```
                    saved answer sets no longer valid
NEWS 14  Jul 29  Enhanced polymer searching in REGISTRY
NEWS 15  Jul 30  NETFIRST to be removed from STN
NEWS 16  Aug 08  CANCERLIT reload
NEWS 17  Aug 08  PHARMAMarketLetter (PHARMAML) - new on STN
NEWS 18  Aug 08  NTIS has been reloaded and enhanced
NEWS 19  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                 now available on STN
NEWS 20  Aug 19  IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21  Aug 19  The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22  Aug 26  Sequence searching in REGISTRY enhanced
NEWS 23  Sep 03  JAPIO has been reloaded and enhanced
NEWS 24  Sep 16  Experimental properties added to the REGISTRY file
NEWS 25  Sep 16  Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26  Sep 16  CA Section Thesaurus available in CAPLUS and CA
NEWS 27  Oct 01  CASREACT Enriched with Reactions from 1907 to 1985
NEWS 28  Oct 21  EVENTLINE has been reloaded
NEWS 29  Oct 24  BEILSTEIN adds new search fields
NEWS 30  Oct 24  Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 31  Oct 25  MEDLINE SDI run of October 8, 2002
NEWS 32  Nov 18  DKILIT has been renamed APOLLIT
NEWS 33  Nov 25  More calculated properties added to REGISTRY
NEWS 34  Dec 02  TIBKAT will be removed from STN
NEWS 35  Dec 04  CSA files on STN
NEWS 36  Dec 17  PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 37  Dec 17  TOXCENTER enhanced with additional content
NEWS 38  Dec 17  Adis Clinical Trials Insight now available on STN
NEWS 39  Dec 30  ISMEC no longer available

NEWS EXPRESS  December 31 CURRENT WINDOWS VERSION IS V6.01a,
              CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
              AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
NEWS HOURS    STN Operating Hours Plus Help Desk Availability
NEWS INTER    General Internet Information
NEWS LOGIN    Welcome Banner and News Items
NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:35:02 ON 16 JAN 2003

=> file medline embase biosis scisearch caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               1.21       1.21

FILE 'MEDLINE' ENTERED AT 12:35:17 ON 16 JAN 2003

FILE 'EMBASE' ENTERED AT 12:35:17 ON 16 JAN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V. All rights reserved.

FILE 'BIOSIS' ENTERED AT 12:35:17 ON 16 JAN 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC. R
```

```
FILE 'SCISEARCH' ENTERED AT 12:35:17 ON 06 JAN 2003
COPYRIGHT (C) 2003 Institute for Scientific Information (ISI) (R)

FILE 'CAPLUS' ENTERED AT 12:35:17 ON 06 JAN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

=> s antibody
L1      2383121 ANTIBODY

=> s l1 and CD23
L2         3262 L1 AND CD23

=> s l2 and human IgG1 constant
L3            0 L2 AND HUMAN IGG1 CONSTANT

=> s l2 and IgG1
L4          182 L2 AND IGG1

=> s l4 and human
   4 FILES SEARCHED...
L5           76 L4 AND HUMAN

=> s l5 and inhibit IgE
L6            0 L5 AND INHIBIT IGE

=> dup remove l4
PROCESSING COMPLETED FOR L4
L7           67 DUP REMOVE L4 (115 DUPLICATES REMOVED)

=> d l7 1-67 cbib abs

L7   ANSWER 1 OF 67     MEDLINE                                  DUPLICATE 1
2001506103  Document Number: 21429293.    PubMed ID: 11544299.   Regulation of
     IgE production requires oligomerization of CD23. Kilmon M A;
     Ghirlando R; Strub M P; Beavil R L; Gould H J; Conrad D H. (Department of
     Microbiology and Immunology, Virginia Commonwealth University, Richmond,
     VA 23298, USA.. mkilmon@hsc.vcu.edu) . JOURNAL OF IMMUNOLOGY, (2001 Sep
     15) 167 (6) 3139-45.  Journal code: 2985117R. ISSN: 0022-1767. Pub.
     country: United States. Language: English.
AB   Here we describe the production of a rabbit polyclonal Ab (RAS1) raised
     against the stalk of murine CD23. RAS1 inhibits release of
     CD23 from the surface of both M12 and B cells resulting in an
     increase of CD23 on the cell surface. Despite this increase,
     these cells are unable to bind IgE as determined by FACS. CD23
     has previously been shown to bind IgE with both a high (4-10 x 10(7)
     M(-1)) and low (4-10 x 10(6) M(-1)) affinity. Closer examination by direct
     binding of (125)I-IgE revealed that RAS1 blocks high affinity binding
     while having no effect on low affinity binding. These data support the
     model proposing that oligomers of CD23 mediate high affinity IgE
     binding. These experiments suggest that RAS1 binding to cell surface
     CD23 results in a shift from oligomers to monomers, which,
     according to the model, only bind IgE with low affinity. These experiments
     also suggest that high affinity binding of IgE is required for IgE
     regulation by CD23 and is demonstrated by the fact that
     treatment of Ag/Alum-immunized mice treated with RAS1 results in a
     significant increase in IgE production similar to the levels seen in
     CD23-deficient mice. These mice also had significantly decreased
     levels of serum soluble CD23 and Ag-specific IgG1.
     RAS1 had no effect on IgE or Ag-specific IgG1 production in
     CD23-deficient mice.
```

L7 ANSWER 2 OF 67 MEDLINE DUPLICATE 2
2001241311 Document Number: 21241546. PubMed ID: 11345290. Clinical and immunologic changes after allergen immunotherapy with Hop Japanese pollen. Park H S; Nahm D H; Kim H Y; Suh Y J; Cho J W; Kim S S; Lee S K; Jung K S. (Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Korea.. hspark@madang.ajou.ac.kr) . ANNALS OF ALLERGY, ASTHMA, AND IMMUNOLOGY, (2001 Apr) 86 (4) 444-8. Journal code: 9503580. ISSN: 1081-1206. Pub. country: United States. Language: English.

AB BACKGROUND AND OBJECTIVE: Hop Japanese (Hop J) pollen has been reported as one of the major causative pollen allergens in the autumn season. There have been no published data regarding the clinical and immunologic effects of Hop J pollen immunotherapy in sensitized patients. In this study, we evaluated clinical and immunologic effects of Hop J immunotherapy. PATIENTS AND METHODS: Pollens were collected in our area, and "Depo-Hop J" was prepared in the laboratory of Allergopharma (Reinbek, Germany). Fifteen asthmatic patients who had Hop J immunotherapy for > 1 year were enrolled. Their clinical parameters, such as asthma symptom scores, were monitored. Skin reactivity to Hop J and degree of airway hyperresponsiveness to methacholine were measured before and 1 year after the immunotherapy. Sera were collected before the immunotherapy, at the end of initial therapy, and 1 year after the therapy. Serum total IgE levels were compared by radioimmunoassay. Serum-specific IgE, **IgG1** , and IgG4 levels to Hop J were compared by ELISA. To evaluate the changes of cellular mechanisms, soluble CD30 (sCD30), soluble interleukin (IL)-2 receptor (sIL-2R), soluble **CD23** (sCD23), and IL-10 levels were measured by ELISA. RESULTS: Specific **IgG1** and IgG4 levels began to increase at the end of the initial therapy ($P < 0.05$) with significant decreases in symptom scores ($P < 0.05$), whereas total and specific IgE levels showed variable responses during the immunotherapy with no statistical significance ($P > 0.05$). Serum sIL-2R and sCD30 levels decreased significantly ($P < 0.05$) 1 year after immunotherapy. No significant changes were noted in sCD23, IL-10, skin reactivity to Hop J, or airway responsiveness to methacholine ($P > 0.05$). CONCLUSIONS: We are certain that Hop J allergen immunotherapy, if carried out properly according to suitable indications, can favorably influence asthma. Thus, an increase in specific IgG4 and **IgG1 antibodies** and reduction of a possible Th2 lymphocyte marker (sCD30) may be associated with symptomatic improvements.

L7 ANSWER 3 OF 67 SCISEARCH COPYRIGHT 2003 ISI (R)
2001:329090 The Genuine Article (R) Number: 420KX. IgE-mediated suppression of primary **antibody** responses in vivo. Karlsson M C I; De Stahl T D; Heyman B (Reprint). Uppsala Univ, Rudbeck Lab, Dept Genet & Pathol, SE-75185 Uppsala, Sweden (Reprint). SCANDINAVIAN JOURNAL OF IMMUNOLOGY (APR 2001) Vol. 53, No. 4, pp. 381-385. Publisher: BLACKWELL SCIENCE LTD. P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND. ISSN: 0300-9475. Pub. country: Sweden. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The ability of immunoglobulin (Ig)G to feedback suppress **antibody** (Ab) responses is a well known property clinically used to prevent haemolytic disease of newborns. We recently found that IgG was able to suppress the primary Ab response to sheep red blood cells (SRBC) in mice lacking the known Fc-receptors for IgG. In addition, IgE and F(ab')2 fragments of IgG were able to suppress the response to SRBC in wild-type mice. These results suggested that the IgG-mediated suppression can take place independently of the IgG Fc portion and that masking of the epitopes is an important mechanism. In the present report we investigated whether the suppression caused by IgE is Fc-dependent. Monoclonal IgE anti-2,4,6-trinitrophenyl (TNP), administered with TNP-coupled SRBC (SRBC-TNP), can induce an efficient suppression in mice lacking Fc gamma RI + RIII + Fc epsilon RI owing to the lack of the common gamma chain, FcR gamma, Fc gamma RIIB or Fc epsilon RII

CD23,. Because the known IgE-binding receptors are Fc epsilon RI, **CD23**, Fc gamma RIIB and Fc gamma RIII, the results suggest that also the IgE-mediated suppression can take place independently of the Fc-receptors. A slightly less efficient suppression in **CD23** -deficient animals, suggests a minor involvement of this receptor.

L7 ANSWER 4 OF 67 CAPLUS COPYRIGHT 2003 ACS
2000:592919 Document No. 133:192004 Assay for the identification of IgE **antibody** suppressors. Katz, David H. (USA). PCT Int. Appl. WO 2000049409 A2 20000824, 21 pp. DESIGNATED STATES: W: CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US3885 20000215. PRIORITY: US 1999-251175 19990217.
AB The invention provides an IgE and antigen-specific screening assay for use in identifying agents which suppress the IgE mediated immune response to antigen. The assay is performed in vivo in Animals which hyper respond to antigen by producing exaggerated levels of IgE. The animals are sensitized to an antigen during a specific window of sensitivity which closes a day after the animal has been treated to produce the IgE hyper responsive phenotype. The screening assay is performed in the animals by treating them with a candidate IgE suppressor agent in conjunction with further immunization made after closure of the window of sensitivity defined by the invention. Pos. results (indicating that the candidate agent has IgE suppressive activity) are obtained in the assay through measurement of a decline in antigen-specific IgE in the animal following its treatment with the candidate agent. The screening assay may also be utilized to measure other components of the immune response to antigen, including **IgG1** and IgG2a **antibody** prodn.

L7 ANSWER 5 OF 67 CAPLUS COPYRIGHT 2003 ACS
2000:457197 Document No. 133:57697 Enhanced proteins production in cell culture stimulated by unusually low alkanoic acid concentrations. Islam, Seema; Sharp, Nigel Alan (Glaxo Group Limited, UK). PCT Int. Appl. WO 2000039282 A1 20000706, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP10157 19991221. PRIORITY: GB 1998-28624 19981223.
AB A process is provided for the prodn. of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium contg. an alkanoic acid or its salt at a maintained concn. of less than 0.1mM. Thus, NSO cells transfected with an **IgG1** humanized anti-**CD23 antibody** was cultured for 56 days in a draw and fill repeated batch mode in a medium contg. 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.075mM butyrate showed a marked increase in **antibody** prodn. over the control.

L7 ANSWER 6 OF 67 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 3
2000115522 EMBASE **CD23** exhibits negative regulatory effects on allergic sensitization and airway hyperresponsiveness. Haczku A.; Takeda K.; Hamelmann E.; Loader J.; Joetham A.; Redai I.; Irvin C.G.; Lee J.J.; Kikutani H.; Conrad D.; Gelfand E.W.. Dr. E.W. Gelfand, Department of Pediatrics, Natl. Jewish Med. and Res. Center, 1400 Jackson Street, Denver, CO 80206, United States. American Journal of Respiratory and Critical Care Medicine [illegible]
Refs: 35.
ISSN: 1073-449X. CODEN: AJRMEL. Pub. Country: United States. Language: English. Summary Language: English.
AB The effects of an anti-**CD23** monoclonal **antibody** B3B4

in **CD23**-deficient and **CD23**-overexpressing mice were compared in a murine model of allergic sensitization. After sensitization and challenge with OA, mice developed increased serum levels of OA-specific IgE and **IgG1** with airway eosinophilia and AHR when compared with nonsensitized animals. Anti-**CD23** treatment was studied under two protocols: 10-d OA aerosol exposure and intraperitoneal sensitization followed by aerosol challenge. In both protocols anti-**CD23** significantly reduced IgE and **IgG1** levels, abolished eosinophilia, and normalized AHR in BALB/c and wild-type **CD23**(+/+) mice but not in **CD23**(-/-) mice. These changes were associated with increases in IFN-.gamma. and decreases in IL-4 production, suggesting that **CD23** binding may affect not only IgE production but also the Th1/Th2 imbalance during the development of allergic AHR. Absence of **CD23** in gene-deficient mice significantly enhanced OA- specific IgE and **IgG1** levels, airway eosinophilia, and AHR when compared with **CD23**(+/+) wild-type littermates after sensitization and airway challenge. Sensitized and challenged **CD23** transgenic mice also developed eosinophilic airway inflammation and methacholine hyperresponsiveness. However, the extent of AHR, BAL, and tissue eosinophilia in these animals showed a significant negative correlation with levels of **CD23** expression on splenic T and B cells, demonstrating a limiting role of **CD23** in the development of allergic AHR.

L7 ANSWER 7 OF 67 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

2000351437 EMBASE Historical views of interleukin studies: IL-4. Hamuro J.. Dr. J. Hamuro, Basic Research Institute, Ajinomoto Co., Inc., 1-1 Suzuki-cho, Kawasaki-ku, Kawasaki 210-0801, Japan. Biotherapy 14/8 (819-834) 2000.
Refs: 91.
ISSN: 0914-2223. CODEN: BITPE. Pub. Country: Japan. Language: Japanese. Summary Language: English; Japanese.

AB Mature human IL-4 is composed of 129 amino acids, and it contains 4 .alpha.-helix structures. Its chromosomal gene is located in 5q31.1 together with GM-CSF, IL-3, IL-9, IL-13 and IRF-1, all of which participate in hematopoiesis. IL-4 is produced mainly by Th2 cells, although basophils, mast cells, CD4+ NK1.1 T cells, CD4-CD8- T cells and .gamma. .delta. + T cells are also able to produce it under appropriate conditions. The CD28/CD80, 86 interaction induces IL-4 production and that of LFA-1/ICAM reduces it. CD4+ NK1.1 T cells are known to produce a large amount of IL-4, playing a pivotal role in the differentiation of Th0 to Th2. PGE2 inhibits the induction of Th2, whereas corticosteroids inhibit its production by mast cells but augment that by monocytes. The IL-4 gene contains promoter regions called P0, P1, P2, P3 and P4. A transcription factor, NF-ATp, binds to P4 and Th2-specific P1. On the other hand NF-ATc, Fos and Oct1/2 bind to P0/Oct, while Th2-specific c-maf binds to the MARE sequence. In the presence of TGF-.beta., IL-4 induces the differentiation to Th1 from Th0. IL-4 differentiates CD8+ T cells to Tc2, Which is capable of producing IL-4, IL-5 and IL-10, or to cytotoxic Tc1, depending on the absence or presence of TGF-.beta.. An IL-4 receptor is expressed on all hematopoietic cells, hepatocytes, fibroblasts, keratinocytes and on certain neuronal cells. It consists of an .alpha. chain and an IL-2R .gamma. c chain as a heterodimer. Upon IL-4 triggering, Jak1 and Jak3 are activated, and IRS-1/2 are phosphorylated. Phosphorylated Stat6 homodimerizes, translocates into the nucleus and activates genes such as **CD23**, MHC class II, C .epsilon., C .gamma., I and c-fes. It also induces the augmented expression of IL-4R.alpha.. IL-4 plays a relevant role in the switching of **antibody** isotype to **IgG1** and IgE, suppression of the diverse monocyte/M .phi. functions, chemotaxis of inflammatory cells by the chemokine induction and augmentation of chemokine receptors. Many aspects of the role of IL-4 in autoimmune and atopic disease progression are discussed herein.

L7 ANSWER 8 OF 67 MEDLINE DUPLICATE 4
2000436821 Document Number: 20420775. PubMed ID: 10963809. Absence of interleukin-4 enhances germinal center reaction in secondary immune response. Andoh A; Masuda A; Yamakawa M; Kumazawa Y; Kasajima T. (Department of Pathology, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666, Tokyo, Japan.. ando@research.twmu.ac.jp) . IMMUNOLOGY LETTERS, (2000 Jul 3) 73 (1) 35-41. Journal code: 7910006. ISSN: 0165-2478. Pub. country: Netherlands. Language: English.

AB The germinal center (GC) is a compartment for B cell differentiation and proliferation. Interleukin (IL)-4 has been considered essential for GC functioning. To define the role of IL-4 in GC reaction, immunohistology of draining lymph nodes (LNs) of IL-4 gene-targeted (IL-4(-/-)) mice was performed during secondary immune response. IL-4(-/-) mice were immunized with ovalbumin emulsified in Freund' complete adjuvant. Final antigen challenge was done 4 weeks later. IL-4(-/-) mice had a higher production of IgG2a and IgG2b and a lower production of **IgG1** than those in wild-type (WT) mice. In comparison with WT mice, LNs of IL-4(-/-) mice on days 4 and 7 after final antigen challenge were larger and contained a markedly greater number of GCs, which showed marked size variations with a large number of small GCs and a small number of markedly large GCs. By day 14, the number of GCs decreased to the same level as that in WT mice. However, the LN size in IL-4(-/-) mice was still larger than that in WT mice due to the presence of markedly large GCs. Although well-developed complement receptor(+) follicular dendritic cell (FDC) networks were present in GCs of IL-4(-/-) mice, no FDCs of mature phenotype (**CD23**(+)) were observed in many of the small GCs. In conclusion, the absence of IL-4 enhanced GC reaction and specific **antibody** response of Th1-type. IL-4 may play an important role in inducing the appropriate magnitude of humoral immune response.

L7 ANSWER 9 OF 67 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**.
Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized **IgG1** , with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

L7 ANSWER 10 OF 67 MEDLINE DUPLICATE 5
99316807 Document Number: 99316807. PubMed ID: 10384119. Humoral response suppression observed with **CD23** transgenics. Payet M E; Woodward E C; Conrad D H. Department of Microbiology and Immunology, Virginia Commonwealth University, Richmond 23298, USA.. JOURNAL OF IMMUNOLOGY, 1999 Jul 1 163 1 217-23. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB **CD23**, also known as the low affinity IgE receptor FcepsilonRII , has been hypothesized to have a role in IgE regulation. A new **CD23** transgenic mouse was generated using the MHC class I

promoter and IgH enhancer to further test the hypothesis that **CD23** plays a role in the down-regulation of IgE. Study of three founder lines by FACS showed overexpression to varying extents on both B and T lymphocytes. No alterations in lymphocyte populations was observed. All three founder lines exhibited strong suppression of IgE in response to DNP-keyhole limpet hemocyanin/alum and Nippostrongylus brasiliensis infection compared with that in parental or littermate controls. The founder line exhibiting the highest level of suppression also was less susceptible to Ag-induced systemic anaphylactic shock. Overall, the data support the concept that enhancing **CD23** levels can be used to suppress IgE-mediated disease. The mechanism involves decreased IgE synthesis, because the serum half-life of IgE was not altered in transgenics, and enzyme-linked immunospot analysis demonstrated lower IgE-producing cells stimulated by injection of anti-IgD. Transgenics also exhibited significantly decreased **IgG1** responses and exhibited lower levels of all Ig isotypes, although this was more variable in different founder lines.

L7 ANSWER 11 OF 67 MEDLINE DUPLICATE 6

1999111232 Document Number: 99111232. PubMed ID: 9893160. Upregulated surface expression of intracellularly sequestered Igepsilon receptors (FcepsilonRII/**CD23**) following activation in human peripheral blood eosinophils. Sano H; Munoz N M; Sano A; Zhu X; Herrnreiter A; Choi J; Leff A R. (Department of Medicine, Section of Pulmonary and Critical Care Medicine.) PROCEEDINGS OF THE ASSOCIATION OF AMERICAN PHYSICIANS, (1999 Jan-Feb) 111 (1) 82-91. Journal code: 9514310. ISSN: 1081-650X. Pub. country: United States. Language: English.

AB We investigated the regulation, secretion, and surface expression of the low-affinity FcepsilonRII receptor (**CD23**) in eosinophils isolated from human blood using multiple monoclonal **antibodies** (mAbs) directed at different epitopes of human **CD23**. Substantial surface expression of **CD23** was not demonstrated in the resting state. Mean fluorescence intensity (MFI) measured by flow cytometry was 7.1 +/- 0.8 for 9P25 mAb (p = NS) and 15.7 +/- 3.8 for BU38 mAb (p <. 04) versus 5.3 +/- 1.0 for **IgG1** isotype control Ab. By contrast, MFI using BU38 mAb was 154 +/- 18 for JY-B lymphocytes (p <.0001 versus eosinophils). Despite weak surface expression, eosinophil permeabilization demonstrated substantial intracellular expression of **CD23**; MFI was 33.6 +/- 5.2 for 9P25 mAb versus 4.4 +/- 0.43 for IgG control (p <.001). Western blot analysis using both positive and negative controls demonstrated immunological identity with **CD23** on JY-B lymphocytes. Activation of eosinophils caused rapid translocation of **CD23** to the surface membrane (160 +/- 33 MFI; p <. 005), which was maximal within 30 sec. Secretory **CD23** was detected within the perfusate also at 30 sec and was fully reinternalized at 10 min. This is the first demonstration of the presence of intracellular **CD23** in human eosinophils. Our data indicate that eosinophils rarely express **CD23** on their surface but are capable of transient high-level expression and secretion with rapid reuptake of intracellular stores of **CD23**.

L7 ANSWER 12 OF 67 MEDLINE DUPLICATE 7

1999101463 Document Number: 99101463. PubMed ID: 9886372. Mouse IL-13 enhances **antibody** production in vivo and acts directly on B cells in vitro to increase survival and hence **antibody** production. Lai Y H; Mosmann T R. Department of Medical Microbiology and Immunology, University of Alberta, Edmonton, Canada. JOURNAL OF IMMUNOLOGY, (1999 Jan 1) 162 (1) 79-87. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB IL-13, a Th2 cytokine, exhibits similar functions to IL-4 in stimulating proliferation and class switching of human B cells. Although mouse B cells were reported to be unresponsive to IL-13, we now show that IL-13 directly stimulates mouse B cells, causing extended survival and higher Ab levels.

Recombinant mouse IL-13 was administered via osmotic pump during immunization of BALB/c mice with chicken RBCs. IL-13 treatment enhanced not only the plasma levels of total **IgG1**, IgG2a, and IgG2b but also Ag-specific Ig levels. To examine whether IL-13 acted directly on mouse B cells, B220+ B cells were cultured with fixed, anti-CD3-activated Th2 clones. Production of IgM and **IgG1** was enhanced moderately by IL-13 and strongly by IL-4. Anti-CD40-stimulated sIgD+ mouse B cells also responded to IL-13 by producing increased levels of IgM, and to a lesser extent **IgG1**, IgG2a, IgG2b, and IgG3. No evidence was found for IL-13-induced class switching. Mouse B cells were stimulated directly rather than indirectly via contaminating cells, as IL-13 increased the numbers of both total and Ab-secreting B cells in aliquots of 100 sIgD+ B cells (>99.5% pure) stimulated with anti-CD40 Ab. Stimulation of B cells by IL-13 was unaffected by the addition of anti-IL-4 to the cultures. In contrast to IL-4, IL-13 did not increase **CD23** expression or B cell proliferation as measured by dilution of an intracellular fluorescence label. Collectively, these data indicate that IL-13 can enhance mouse B cell Ab production by increasing survival of the B cells.

L7 ANSWER 13 OF 67 SCISEARCH COPYRIGHT 2003 ISI (R)
1998:146156 The Genuine Article (R) Number: YW267. Presence of activated antigen-binding B cells during immunization enhances relative levels of IFN-gamma in T cell responses. Pasare C; Morafo V; Entringer M; Bansal P; George A; Bal V; Rath S (Reprint); Durdik J M. NATL INST IMMUNOL, NEW DELHI 110067, INDIA (Reprint); NATL INST IMMUNOL, NEW DELHI 110067, INDIA; UNIV ARKANSAS, DEPT BIOL SCI, FAYETTEVILLE, AR 72701. JOURNAL OF IMMUNOLOGY (15 JAN 1998) Vol. 160, No. 2, pp. 778-787. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767. Pub. country: INDIA; USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB To examine the influence of Ag presentation by B cells on immune responses, we have used mice transgenic for an Ig heavy chain from a monoclonal anti-azobenzenearsonate (Ars) Ab to deliver Ag to B cells during immunization, A large proportion of transgene-expressing B cells in these mice binds Ars, while transgenic serum Ig shows poor Ars binding. Transgenic B cells present Ars proteins better than their nonhaptenated counterparts. This is associated with an increase in the proliferative responses of transgenic T cells to Ars protein immunization, Although B cell numbers in the transgenic mice are lower, many B cells in them show an activated phenotype, as identified by altered surface levels of peanut agglutinin reactivity, **CD23**, CD24, CD44, CD62L, and CD86. Even against nonhaptenated immunogens, transgenic responses show significant enhancement in the relative proportions of the Th1 cytokine IFN-gamma over the Th2 cytokines IL-4 and IL-10. Haptenated immunogens further enhance the predilection of transgenic mice to produce relatively more IFN-gamma. Consistent with this, there is an increase in IgG2a/**IgG1** ratios in serum Abs in response to haptenated immunogens in transgenic mice, Adoptive transfer of primed hapten-specific secondary B cells into nontransgenic mice also induces an increase in relative levels of IFN-gamma in response to haptenated immunogens, Thus, presentation of immunogen in vivo by activated Ag-binding B cells contributes to enhanced immunogenicity and a Th1 cytokine bias.

L7 ANSWER 14 OF 67 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 9
1998312114 EMBASE Inhibition of sCD23 and immunoglobulin E release from human B cells by a metalloproteinase inhibitor, GI 129471. Wheeler D.C.; Parveen S.; Pollock K.; Williams R.O.. Dr. D.C. Wheeler, Department of Cell Biology, Rhone-Poulenc-Rorer Ltd, Dagenham Research Centre, Dagenham, Essex RM10 7XS, United Kingdom. Immunology 95 1 105-111 1998.
Refs: 21.
ISSN: 0019-2805. CODEN: IMMUAM. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Soluble **CD23** (sCD23) has been proposed to play an important role in the up-regulation of immunoglobulin E (IgE) synthesis. Production of sCD23 is dependent on the proteolytic cleavage of membrane **CD23**, but the protease(s) involved in this process remain unknown. Preliminary data, obtained by testing a panel of protease inhibitors, suggested that this enzyme may be a zinc-dependent metalloproteinase. Therefore, we investigated the effect of a standard hydroxamate-type Zn2+ metalloproteinase inhibitor (GI 129471) on both sCD23 and IgE release from human tonsiltar B cells, stimulated with interleukin-4 (IL-4) and anti-CD40. Incubation of cells for 3 days with GI 129471 inhibited the production of sCD23 with an IC50 of 602 nM .+-. 3 nm (n=3), but by 14 days the activity of the compound against sCD23 had decreased by greater than threefold (IC50 2 .+-. 0.26 .mu.M; n=3). On the other hand, GI 129471 caused a potent inhibition of IgE production, with no apparent loss of activity over the culture period (14 days: IC50 250 nM .+-. 72 nM; n=3). Time-course studies showed that, despite loss of activity against sCD23, inhibition of sCD23 production early in the culture was able to cause a potent and long-lasting inhibitory effect on IgE. Furthermore, we also showed that the activity of GI 129471 is selective for IgE, as no effect was seen on immunoglobulin G1 (**IgG1**) or IgG4 production at test concentrations as high as 10 .mu.M. These results support the hypothesis that metalloproteinases may be involved in the proteolytic cleavage of **CD23** and subsequent regulation of IgE synthesis. Inhibition of the protease(s) responsible for such cleavage may be of value in the treatment of allergic disease.

L7 ANSWER 15 OF 67 SCISEARCH COPYRIGHT 2003 ISI (R)
1998:315648 The Genuine Article (R) Number: ZH754. Control of IgE responses. V. Oral administration of a synthetic derivative of the inner bacterial cell wall (SDZ 280.636) to sensitized mice induces isotype specific suppression of peak hapten specific IgE **antibody** forming cell responses, serum IgE levels and immediate hypersensitivity responses.. Auci D L (Reprint); Kleiner G I; Chice S M; Athanassiades T J; Dukor P; Durkin H G. SUNY HLTH SCI CTR, DEPT PATHOL, BROOKLYN, NY 11203 (Reprint); SANDOZ GMBH, FORSCHUNGSINST, A-1235 VIENNA, AUSTRIA. IMMUNOLOGICAL INVESTIGATIONS (MAR 1998) Vol. 27, No. 1-2, pp. 105-120. Publisher: MARCEL DEKKER INC. 270 MADISON AVE, NEW YORK, NY 10016. ISSN: 0882-0139. Pub. country: USA; AUSTRIA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB SDZ 280.636, a nontoxic diacyl glycerol derivative of muramyl dipeptide (MDP), a component of the inner bacterial cell wall, which is suitable for use in man, suppressed hapten specific IgE **antibody** forming cell (AFC) responses in spleen, serum levels of hapten specific IgE and hapten specific immediate hypersensitivity (IH) responses in skin, when fed to mice at the peak of a hapten specific IgE AFC response. In addition, serum levels of IL-6 appeared increased while IFN gamma was decreased. To induce these IgE responses, BALB/c mice were injected i.p. with BPO-KLH (benzylpenicilloyl-keyhole limpet hemocyanin) (10 mu g) in aluminum hydroxide gel (alum) on days 0, 21 and 42. Mice were fed (gavage) with either MDP or SDZ 280.636 (1.0 or 10 mg/kg) on day 44, or on days 44, 46 and 48, and killed on days 46 or 50, Numbers of BPO specific AFC in spleen, and serum levels of BPO specific immunoglobulins (**IgG1**, IgE and IgA) were determined (ELISPOT assay, ELISA). In addition, BPO specific IH responses were measured in these animals. Mice were injected in the right pinna with BPO-BSA (0.1 mu g) and in the left pinna with an equal volume of saline (0.05 ml). At 2 hr, pinnae were measured using a micrometer caliper. We found that 1 feeding with either MDP or SDZ 280.636 abrogated IgE AFC responses and dramatically suppressed serum levels of IgE, both in isotype specific fashion, and suppressed IH responses (>80%). 3 feedings with SDZ 280.636 also abrogated IgE AFC responses and further decreased serum levels of IgE. In contrast to SDZ 280.636, 3 treatments with MDP had opposite effects in that IgE AFC responses and serum levels of IgE dramatically increased. A single treatment with SDZ 280.636

appeared to increase serum levels of IL-6 up to three fold, while IFN gamma levels decreased. Our data suggest that SDZ 280.636 may be useful in the therapeutic and prophylactic management of human atopic disease such as allergic rhinitis, asthma, and other atopic diseases.

L7 ANSWER 16 OF 67 MEDLINE DUPLICATE 9
1998382632 Document Number: 98382632. PubMed ID: 9716904. K21-antigen: a molecule shared by the microenvironments of the human thymus and germinal centers. Imami N; Ladyman H M; Vincents B; al-Tubuly A; Freysdottir J; Sedibane M L; Taylor-Fishwick D A; Foxwell B M; Ritter M A. (Department of Immunology, Imperial College School of Medicine, Hammersmith Hospital, London, United Kingdom.) DEVELOPMENTAL IMMUNOLOGY, (1998) 6 (1-2) 41-52. Journal code: 9200624. ISSN: 1044-6672. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The mouse **IgG1** monoclonal **antibody** (mAb) K21 recognizes a 230-kD molecule (K21-Ag) on Hassall's corpuscles in the human thymus. This mAb also stains cultured thymic epithelial cells as well as other epithelial cell lines, revealing a predominant intracellular localization. Further analysis with mAb K21 on other lymphoid tissues showed that it also stains cells within the germinal centers of human tonsils, both lymphoid (B) cells and some with the appearance of follicular dendritic cells. Double immunostaining of tonsil sections shows that K21-Ag is not expressed by T cells, whereas staining with anti-CD22 and -**CD23** mAb revealed some double-positive cells. A subpopulation of the lymphoid cells express the K21-Ag much more strongly. This K21++/**CD23**++ subpopulation of cells is localized in the apical light zone of germinal centers, suggesting that K21-Ag may be an important marker for the selected centrocytes within germinal centers and may play a role in B-cell selection and/or development of B-cell memory. Flow cytometric analysis showed that K21-Ag is expressed on the surface of a very low percentage of thymocytes, tonsillar lymphocytes, and peripheral blood mononuclear cells. Analysis of purified/separated tonsillar T and B lymphocytes showed that T cells do not express the K21-Ag; in contrast, B cells express low levels of the K21-Ag, and this together with **CD23** is upregulated after mitogenic stimulation. Our data therefore raise the possibility that the K21-Ag may play a role in B-lymphocyte activation/selection.

L7 ANSWER 17 OF 67 SCISEARCH COPYRIGHT 2003 ISI (R)
97:760655 The Genuine Article (R) Number: XZ994. Modulation of antigen-induced B and T cell responses by antigen-specific IgE **antibodies**. Oshiba A; Hamelmann E; Haczku A; Takeda K; Conrad D H; Kikutani H; Gelfand E W (Reprint). NATL JEWISH MED & RES CTR, DEPT PEDIAT, DIV BASIC SCI, 1400 JACKSON ST, DENVER, CO 80206 (Reprint); NATL JEWISH MED & RES CTR, DEPT PEDIAT, DIV BASIC SCI, DENVER, CO 80206; VIRGINIA COMMONWEALTH UNIV, MED COLL VIRGINIA, DEPT MICROBIOL & IMMUNOL, RICHMOND, VA 23298; OSAKA UNIV, INST MOL & CELLULAR BIOL, SUITA, OSAKA 565, JAPAN. JOURNAL OF IMMUNOLOGY (15 OCT 1997) Vol. 159, No. 8, pp. 4056-4063. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767. Pub. country: USA; JAPAN. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Ag-specific IgE Abs not only mediate immediate hypersensitivity through mast cell activation, but also enhance in vitro Ag presentation and in vivo specific Ab responses in mice. To delineate the role of IgE Ab in the modulation of Ag-specific responses, spleen cells from OVA-sensitized BALB/c mice were cultured together with OVA-specific IgE or IgG isotypes. OVA-dependent proliferative responses and anti-OVA IgE production were enhanced in the presence of anti-OVA IgE. A significant decrease in IFN-gamma secretion in OVA-stimulated cultures was observed in the presence of anti-OVA IgE, but no changes in IL-4 production were detected. Anti-OVA Ige isotypes or anti-TNP IgE showed no significant effect on any of these Ag-dependent responses. Addition of anti-

CD23 Ab abolished these effects of anti-OVA IgE. Further, OVA-sensitized spleen cells from **CD23**-deficient mice responded to in vitro stimulation with OVA, but demonstrated no modulation by anti-OVA IgE. These results demonstrate that Ag-specific IgE not only augments Ag presentation and T cell proliferation, but also alters the pattern of cytokine production and increases specific IgE synthesis, These modulatory effects of Ag-specific IgE appear to be mediated by binding to Fc epsilon RII/**CD23**.

L7 ANSWER 18 OF 67 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1998:94080 Document No.: PREV199800094080. A new set of monoclonal **antibodies** against human FcgammaRII (CD32) and FcgammaRIII (CD16): Characterization and use in various assays. Vely, Frederic; Gruel, Nadege; Moncuit, Janine; Cochet, Olivier; Rouard, Helene; Dare, Sophie; Galon, Jerome; Sautes, Catherine; Fridman, Wolf-Herman; Teillaud, Jean-Luc (1). (1) Unite INSERM 255, Lab. Biotechnol. Anticorps, Inst. Curie, 26 rue d'Ulm, 75248 Paris Cedex 05 France. Hybridoma, (Dec., 1997) Vol. 16, No. 6, pp. 519-528. ISSN: 0272-457X. Language: English.

AB Four mouse anti-human FcgammaRII (CD32) (6C4,2B2,3D3,93.4) (**IgG1**, kappa) and one anti-human FcgammaRIII (CD16) (7.5.4) (**IgG1**, K) MAbs were raised. An in vitro switch variant, 7.5.4Sw50 (IgG2b, kappa), was also derived from the 7.5.4 MAb. 6C4, 2B2, and 3D3 MAbs bind both FcgammaRIIa and FcgammaRIIb isoforms. Two of them (6C4 and 2B2 MAbs) allow a complete blockade of the binding of immune complexes to FcgammaRII. All three MAbs immunoprecipitate the receptor and bind both its glycosylated and nonglycosylated forms. The fourth antiFcgammaRII MAb, 93.4, directed against the intracellular region of FcgammaRIIa1/2, allows its detection by Western blotting only when it is not phosphorylated. The 7.5.4 MAb binds both FcgammaRIIIa and FcgammaRIIIb, can be used in Western blotting and does not inhibit aggregated IgG binding. ELISA using IV.3 (anti-FcgammaRIIa1/2)/6C4 and 3G8 (anti-FcgammaRIIIa/b)/7.5.4Sw50 MAb pairs make it possible to detect soluble FcgammaRIIa1/2 and FcgammaRIII, with a sensitivity of 200 pg/mL and 1 ng/mL, respectively. Surface plasmon resonance analyses indicated that the KD of two of the three anti-FcgammaRH and of the anti-FcgammaRIII are in the same order of magnitude (6C4: 0.78 nM, 2B2: 0.28 nM, 7.5.4: 0.47 nM). The anti-FcgammaRII 3D3 MAb exhibits an off-rate constant higher than the 6C4 and 2B2 MAbs and a KD of 2.19 nM.

L7 ANSWER 19 OF 67 CAPLUS COPYRIGHT 2003 ACS
1997:77951 Document No. 126:143218 Constitutive expression of interleukin (IL)-4 in vivo causes autoimmune-type disorders in mice. Erb, Klaus J.; rueger, Beate; von Brevern, Maja; Ryffel, Bernhard; Schimpl, Annelise; Rivett, Karen (Malaghan Institute Medical Research, Wellington School Medicine, Wellington South, N. Z.). Journal of Experimental Medicine, 185(2), 329-339 (English) 1997. CODEN: JEMEAV. ISSN: 0022-1007. Publisher: Rockefeller University Press.

AB The transgenic (tg) expression of interleukin (IL)-4 under the control of a major histocompatibility complex (MHC) class I promoter leads to B cell hyperactivity in mice, characterized by increased B cell surface MHC class II and **CD23** expression, elevated responsiveness of the B cells to polyclonal ex vivo stimulation, and increased **IgG1** and IgE serum levels. Tg mice develop anemia, glomerulonephritis with complement and immune deposition in the glomeruli, and show increased prodn. of autoantibodies. Treatment of IL-4 tg mice with anti-IL-4 neutralizing **antibodies** protected the mice from disease development, showing that IL-4 was responsible for the obsd. disorders. Deletion of superantigen responsive autoreactive T cells in the IL-4 tg mice was normal and treatment of mutant mice with deleting anti-CD4 **antibodies** failed to ablate the onset of autoimmune-like disease, suggesting that CD4+ T cells were not the primary cause of the disorders. Furthermore, the deletion of B cells reacting against MHC class I mols. was also normal in the IL-4 tg mice. Therefore the most likely

explanation for the increased prodn. of autoantibodies and the autoimmune-like disorders is that IL-4 acts directly on autoreactive B cells by expanding them in a polyclonal manner. Our results show that inappropriate multi-organ expression of IL-4 in vivo leads to autoimmune-type disease in mice.

L7 ANSWER 20 OF 67 SCISEARCH COPYRIGHT 2003 ISI (R)
96:732679 The Genuine Article (R) Number: VL333. PROSTAGLANDIN E(2) RECEPTORS OF THE EP(2) AND EP(4) SUBTYPES REGULATE ACTIVATION AND DIFFERENTIATION OF MOUSE B-LYMPHOCYTES TO IGE-SECRETING CELLS. FEDYK E R; PHIPPS R P (Reprint). UNIV ROCHESTER, CTR CANC, SCH MED, BOX 704, 601 ELMWOOD AVE, ROCHESTER, NY, 14642 (Reprint); UNIV ROCHESTER, SCH MED & DENT, CTR CANC, DEPT MICROBIOL, ROCHESTER, NY, 14642; UNIV ROCHESTER, SCH MED & DENT, DEPT ENVIRONM MED & PEDIAT, CANC CTR, IMMUNOL PROGRAM, ROCHESTER, NY, 14642; UNIV ROCHESTER, SCH MED & DENT, DEPT ENVIRONM MED & PEDIAT, CANC CTR, THORAC ONCOL PROGRAM, ROCHESTER, NY, 14642. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA (01 OCT 1996) Vol. 93, No. 20, pp. 10978-10983. ISSN: 0027-8424. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Prostaglandin E(2) (PGE(2)) is a potent lipid molecule with complex proinflammatory and immunoregulatory properties. PGE(2) can shape the immune response by stimulating the production of IgE **antibody** by B lymphocytes and the synthesis of T-helper type 2 cytokines [e.g., interleukin (IL)-4, IL-10], while inhibiting production of Th1 cytokines (e.g., interferon-gamma, IL-12). It is unknown what type of receptor binds PGE(2) and modulates these responses. Recent analyses in nonhematopoietic cells have identified six PGE(2) receptors (EP(1), EP(2), EP(3 alpha), EP(3 beta), EP(3 gamma), and EP(4)). This investigation examines quiescent B lymphocytes and reports that these cells express mRNA encoding EP(1), EP(2), EP(3 beta), and EP(4) receptors. The immunoregulatory functions of each receptor were investigated using small molecule agonists that preferentially bind EP receptor subtypes. Unlike agonists for EP(1) and EP(3), agonists that bound EP(2) or EP(2) and EP(4) receptors strongly inhibited expression of class II major histocompatibility complex and **CD23** and blocked enlargement of mouse B lymphocytes stimulated with IL-4 and/or lipopolysaccharide. PGE(2) promotes differentiation and synergistically enhances IL-4 and lipopolysaccharide-driven B-cell immunoglobulin class switching to IgE. Agonists that bound EP(2) or EP(2) and EP(4) receptors also strongly stimulated class switching to IgE. Experiments employing inhibitors of cAMP metabolism demonstrate that the mechanism by which EP(2) and EP(4) receptors regulate B lymphocyte activity requires elevation of cAMP. In conclusion, these data suggest that antagonists to EP(2) and EP(4) receptors will be important for diminishing allergic and IgE-mediated asthmatic responses.

L7 ANSWER 21 OF 67 MEDLINE DUPLICATE 10
97131831 Document Number: 97131831. PubMed ID: 8977305. CD40-mediated stimulation of B1 and B2 cells: implication in autoantibody production in murine lupus. Kaneko Y; Hirose S; Abe M; Yagita H; Okumura K; Shirai T. (Department of Immunology, Juntendo University School of Medicine, Tokyo, Japan.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Dec) 26 (12) 3061-5. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.
AB B1 cells usually show preferential responses to T cell-independent antigens. To ask whether B1 cells could respond to CD40-mediated stimulation for proliferation and differentiation, and whether CD40-mediated signals are involved in the production of autoantibodies by B1 cells, we compared responses to our newly established agonistic anti-mouse CD40 monoclonal **antibody** mAb between B1 and B2 cells from autoimmune-prone NZB x NZW F1 mice. Stimulation with this mAb induced a similar level of proliferative responses of both B1 and B2 cells, as well as an increase in expression of cell surface molecules I-A,

CD54, **CD23**, CD80, and CD86. While co-stimulation with interleukin (IL)-4 markedly augmented proliferative as well as **IgG1** and IgE **antibody** responses of both B and B2 cells, co-stimulation with IL-5 augmented proliferative and IgM **antibody** responses of only B1 cells. Splenic B1, but not B2 cells from young (NZB x NZW) F1 mice spontaneously produced substantial amounts of IgM including IgM anti-DNA **antibodies**, and the levels increased in case of stimulation with anti-CD40 mAb alone, or to a greater extent with the mAb plus IL-4 and IL-5. Collectively, these results indicate that splenic B1 cells from autoimmune (NZB x NZW) F1 mice have a comparable responsiveness to the CD40-mediated stimulation to that of B2 cells, which would be a potent regulatory mechanism involved in the spontaneous production of autoantibodies by B1 cells.

L7 ANSWER 22 OF 67 MEDLINE DUPLICATE 11

96239301 Document Number: 96239301. PubMed ID: 8656055. Development and characterization of a novel monoclonal **antibody** (mNI-11) that induces cell adhesion of the LPS-stimulated human monocyte-like cell line U937. Ikewaki N; Inoko H. (Department of Microbiology, Kitasato University School of Nursing, Kitasato, Sagamihara, Japan.) JOURNAL OF LEUKOCYTE BIOLOGY, (1996 May) 59 (5) 697-708. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.

AB A monoclonal immunoglobulin G1 (**IgG1**) **antibody** (mAb), designated mNI-11, was produced by immunizing mice with the lipopolysaccharide (LPS)-stimulated monocyte-like cell line U937. The reactivity of mNI-11 was tested by the indirect immunofluorescence method. The antigen defined by mNI-11 was found to be expressed on U937 cells, LPS-stimulated U937 cells, normal CD14+ cells (monocytes/macrophages), and human umbilical vein endothelial cells (HUVECs). Expression of the antigen defined by mNI-11 on HUVECs slightly increased in response to exposure to tumor necrosis factor-alpha (TNF-alpha) and phorbol myristate acetate (PMA). When the reactivity of mNI-11 and mAbs binding human differentiation antigens such as CD11a, CD11b, CD11c, CD14, CD16, CD18, **CD23**, CD28, CD29, CD31, CD43, CD44, CD45RA, CD49d, CD50, CD54, CD58, CD80, CD102, CD106, HLA-class I, or HLA-class II antigen was compared, no mNI-11 reactivity resembling that of these mAbs was found. mNI-11 markedly induced homotypic cell aggregation of U937 cells when they were stimulated with LPS. The mNI-11-induced aggregation of LPS-stimulated U937 cells, referred to as LPS-U937 cells, required neither Fc receptor engagement nor cross-linking of the antigen defined by mNI-11 because aggregation was induced by both F(ab')2 fragments and monovalent F(ab') fragments of mNI-11. The mNI-11-induced aggregation was blocked by the addition of ethylenediaminetetraacetate, and also when incubated at 4 degrees C. mAbs to CD11a/CD18 (lymphocyte-function associated antigen-1; LFA-1) and CD54 (intercellular adhesion molecule-1; ICAM-1) completely blocked the LPS-U937 cell aggregation induced by mNI-11. The LPS-U937 cell aggregation induced by mNI-11 was partially but not completely blocked by the protein kinase C inhibitors sphingosine and H-7, and was completely blocked by the protein-tyrosine kinase inhibitor genistein. Interestingly, mNI-11 markedly promoted LPS-U937 cell adhesion to HUVECs. The mNI-11-induced LPS-U937 cell adhesion to HUVECs was not reduced in the presence of LFA-1 (CD11a/CD18) or ICAM-1 (CD54) mAbs. On the other hand, LPS-U937 cells, whether treated with mNI-11 or not, sufficiently adhered to the extracellular matrix protein fibronectin, but not to laminin or collagen type I. However, mNI-11 did not markedly promote LPS-U937 cell adhesion to fibronectin. Adhesion of LPS-U937 cells treated with mNI-11 to fibronectin was completely blocked by CD29 (beta chain of very late antigens) mAb. The surface antigen recognized by mNI-11 had a molecular size of approximately 97 kDa under non-reducing conditions and approximately 117 kDa under reducing conditions, as determined by immunoblotting analysis. We found that mNI-11 recognizes an adhesion-associated molecule distinct from any previously reported in terms of its pattern of cellular distribution and molecular weight, and

also found that mNI-11 has activity which induces cell adhesion/aggregation of U937 cells when stimulated with LPS.

L7 ANSWER 23 OF 67 MEDLINE DUPLICATE 12
96196812 Document Number: 96196812. PubMed ID: 8602263. Essential role of Stat6 in IL-4 signalling. Takeda K; Tanaka T; Shi W; Matsumoto M; Minami M; Kashiwamura S; Nakanishi K; Yoshida N; Kishimoto T; Akira S. (Institute for Molecular and Cellular Biology, Osaka University, Japan.) NATURE, (1996 Apr 18) 380 (6575) 627-30. Journal code: 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Interleukin-4 (IL-4) is a pleiotropic lymphokine which plays an important role in the immune system. IL-4 activates two distinct signalling pathways through tyrosine phosphorylation of Stat6, a signal transducer and activator of transcription, and of a 170K protein called 4PS. To investigate the functional role of Stat6 in IL-4 signalling, we generated mice deficient in Stat6 by gene targeting. We report here that in the mutant mice, expression of **CD23** and major histocompatibility complex (MHC) class II in resting B cells was not enhanced in response to IL-4. IL-4 induced B-cell proliferation costimulated by anti-IgM **antibody** was abolished. The T-cell proliferative response was also notably reduced. Furthermore, production of Th2 cytokines from T cells as well as IgE and **IgG1** responses after nematode infection were profoundly reduced. These findings agreed with those obtained in IL-4 deficient mice or using **antibodies** to IL-4 and the IL-4 receptor. We conclude that Stat6 plays a central role in exerting IL-4 mediated biological responses.

L7 ANSWER 24 OF 67 SCISEARCH COPYRIGHT 2003 ISI (R)
96:685011 The Genuine Article (R) Number: VG477. AUTOANTIBODY-MEDIATED CAPTURE AND PRESENTATION OF AUTOANTIGEN TO T-CELLS VIA THE FC-EPSILON RECEPTOR BY A RECOMBINANT HUMAN AUTOANTIBODY FAB CONVERTED TO IGE. GUO J; QUARATINO S; JAUME J C; COSTANTE G; LONDEI M; MCLACHLAN S M; RAPOPORT B (Reprint). VET ADM MED CTR, THYROID MOL BIOL UNIT 111T, 4150 CLEMENT ST, SAN FRANCISCO, CA, 94121 (Reprint); VET ADM MED CTR, THYROID MOL BIOL UNIT 111T, SAN FRANCISCO, CA, 94121; UNIV CALIF SAN FRANCISCO, SAN FRANCISCO, CA, 94121; MATHILDA & TERENCE KENNEDY INST RHEUMATOL, SUNLEY DIV, LONDON W6 8LW, ENGLAND. JOURNAL OF IMMUNOLOGICAL METHODS (09 SEP 1996) Vol. 195, No. 1-2, pp. 81-92. ISSN: 0022-1759. Pub. country: USA; ENGLAND. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Fc epsilon receptor (**CD23**)-mediated capture of IgE-antigen complexes by B cells provides a powerful antigen presenting system. Our goal was to develop a system using high affinity, human, organ-specific monoclonal autoantibodies for antigen capture by B cells, For this purpose, we converted a recombinant human autoantibody to TPO from a Fab (SP1.4) to an IgE molecule. Sera from all patients with autoimmune thyroid disease contain autoantibodies with the same epitope as SP1.4. The SP1.4 H and L chain V region genes were spliced by overlap PCR to a mammalian, non-immunoglobulin signal peptide and transferred to expression vectors for human **IgG1** and kappa, respectively. After inserting the IgE constant region genes into the H chain vector, the kappa and IgE H chain vectors were expressed in SP2/0 cells. SP1.4-IgE retains its high affinity (K-d for TPO (similar to 2 x 10 -10 M), recognizes the same epitope as Fab SP1.4 and, importantly, binds to a different epitope than does Fab TR1.9. Binding of preformed complexes of SP1.4-IgE and biotinylated TPO to EB virus transformed B cells (EBVL) was weakly detectable by flow cytometry and was displaced by unlabeled TPO. SP1.4-IgE/I-125-TPO complex binding to EBVL was much more clearly evident, was also inhibited by the addition of unlabeled TPO, and was greatly reduced by preincubation of the EBVL with anti-**CD23**. Further, autologous EBVL preincubated with SP1.4-IgE/TPO complexes stimulated proliferation of TPO-specific T cells. IgE autoantibody-mediated antigen focusing to B cells is unlikely to operate in vivo but is, instead, a powerful investigative tool.

In conclusion, SP1.4-IgE is the first monoclonal human autoantibody to be developed for IgE-mediated antigen presentation to T cells by EBVL. Recombinant human autoantibodies converted to IgE, possibly in combinations if their epitopes permit simultaneous binding to the same molecule, provide a unique system to generate human T cell lines and clones specific for peptides naturally processed from internalized high affinity autoantibody/autoantigen complexes.

L7 ANSWER 25 OF 67 MEDLINE DUPLICATE 13
95293053 Document Number: 95293053. PubMed ID: 7774652. No role of interleukin-4 in **CD23**/IgE-mediated enhancement of the murine **antibody** response in vivo. Hjulstrom S; Landin A; Jansson L; Holmdahl R; Heyman B. (Department of Pathology, Uppsala University Hospital, Sweden.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1995 May) 25 (5) 1469-72. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Antigen-specific IgE up-regulates the specific IgM, **IgG1**, IgG2a and IgE response in vivo when given to mice together with antigen. The enhancement is mediated by the low-affinity receptor for IgE, Fc epsilon RII or **CD23**, as demonstrated both in **CD23**-deficient mice and by blocking **CD23** with anti-**CD23** monoclonal **antibodies**. A possible mechanism behind the regulatory effects of **CD23** is that the IgE/**CD23**/antigen complex is endocytosed by B cells, leading to increased antigen processing and presentation on major histocompatibility complex (MHC) class II molecules to T helper cells. In the present study we have found that the expression of **CD23** is reduced fivefold on splenic B cells in mice genetically deficient for IL-4. When IL-4-deficient mice and normal littermates were immunized with 2,4,6-trinitrophenyl (TNP)-specific IgE followed by bovine serum albumin (BSA)-TNP or with BSA-TNP alone, the BSA-specific **IgG1** and IgG2a responses were equally well augmented by IgE in all mice. In addition, a low but significant IgE response was seen even in the IL-4-deficient mice. Thus, enhancement of the **antibody** response through IgE and **CD23** occur in the absence of IL-4 and is not dependent on **CD23** up-regulation.

L7 ANSWER 26 OF 67 MEDLINE DUPLICATE 14
96148598 Document Number: 96148598. PubMed ID: 8550069. Regulation and targeting of T-cell immune responses by IgE and IgG **antibodies**. Bheekha Escura R; Wasserbauer E; Hammerschmid F; Pearce A; Kidd P; Mudde G C. (Department of Immuno-Dermatology, SANDOZ Research Institute, Vienna, Austria.) IMMUNOLOGY, (1995 Nov) 86 (3) 343-50. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A set of chimeric **antibodies** with identical F(ab')2 fragments specific for the hapten 5-iodo-4-hydroxyl-3-nitrophenacetyl (NIP), but with different human Fc parts (gamma 1, gamma 2, gamma 3, gamma 4, epsilon), was used to compare the role of IgG and IgE **antibodies** in antigen presentation by human Epstein-Barr virus (EBV) B cells. Two or three molecules of NIP were coupled to one molecule of Der pI (Der pI-(3)NIP), a major allergen of Dermatophagoides pteronyssinus. Both monomeric IgG and performed complexes of various Der pI/IgG ratios failed to bind significantly to the Fc receptor for IgG on B cells (Fc gamma RII; CD32). Binding of IgG3 > **IgG1** -containing complexes optimal ratio of antigen to **antibody** = 1:1) could be enhanced by increasing the number of haptens per Der pI molecule to nine or more. However, antigen presentation mediated by IgG and CD32 was not seen with either pulsed B cells or B cells that were allowed to capture the IgG complexes during the whole stimulation period. IgE binding to **CD23** and subsequent IgE-mediated antigen presentation was seen under all conditions tested. Even monomeric immune complexes (IC Der pI- 3 NIP/IgE , in the absence of **CD23** cross-linking, induced an immune response. As the number of natural epitopes for human **antibodies** on Der pI was less than five, we conclude that, in

vivo, complexes consisting of Der pI/IgG will be directed to antigen-presenting cells expressing the high-affinity receptor for IgG (CD64), whereas IgE will allow antigen presentation by **CD23** -expressing cells, including B cells.

L7 ANSWER 27 OF 67 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 15
96006044 EMBASE Document No.: 1996006044. Circulating IgG autoanti-IgE **antibodies** in atopic patients block the binding of IgE to its low affinity receptor (**CD23**). Smith S.J.; Jones N.S.; Shakib F.. Div Molecular/Clinical Immunology, University Hospital, Queen's Medical Centre,Nottingham NG7 2UH, United Kingdom. Journal of Clinical Pathology - Clinical Molecular Pathology 48/6 (M342-M346) 1995.
ISSN: 1355-2910. CODEN: JCMPFL. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Aims - To investigate the ability of circulating IgG autoanti-IgE **antibodies** from atopic rhinitis patients to block the binding of IgE to its low affinity receptor (Fc.epsilon.RII), also termed **CD23**. Methods - This involved the use of a well validated flow cytometric method to detect inhibition of FITC labelled IgE binding to human B cells expressing **CD23** (RPMI 8866 cell line). Results - Taking inhibition values greater than 20% as being significant, 15 out of 20 IgG anti-IgE containing sera inhibited the binding of IgE-FITC to the RPMI 8866 cells. The inhibitory effect was recoverable in the IgG fraction of serum, but was not related to the titre of either **IgG1** anti-IgE or IgG4 anti-IgE, thus suggesting that it might be related to epitope specificity. No such inhibition was demonstrable with rheumatoid sera containing autoanti-IgG (that is, rheumatoid factor), but lacking autoanti-IgE. Conclusions - The capacity of anti-IgE to block the binding of IgE to **CD23** has important implications, particularly in terms of upregulation of IgE synthesis and the consequent perpetuation of the inflammatory response.

L7 ANSWER 28 OF 67 MEDLINE
95330828 Document Number: 95330828. PubMed ID: 7606798. Expression and biological activities of bovine interleukin 4: effects of recombinant bovine interleukin 4 on T cell proliferation and B cell differentiation and proliferation in vitro. Estes D M; Hirano A; Heussler V T; Dobbelaere D A; Brown W C. (Department of Veterinary Microbiology, College of Veterinary Medicine, University of Missouri, Columbia 65211, USA.)
CELLULAR IMMUNOLOGY, (1995 Jul) 163 (2) 268-79. Journal code: 1246405.
ISSN: 0008-8749. Pub. country: United States. Language: English.

AB Interleukin 4 (IL-4) is a pleotropic cytokine affecting a wide range of cell types in both the mouse and the human. These activities include regulation of the growth and differentiation of both T and B lymphocytes. The activities of IL-4 in nonprimate, nonmurine systems are not well established. Herein, we demonstrate in the bovine system that IL-4 upregulates production of IgM, **IgG1**, and IgE in the presence of a variety of costimulators including anti-IgM, Staphylococcus aureus cowan strain I, and pokeweed mitogen. IgE responses are potentiated by the addition of IL-2 to IL-4. Culture of bovine B lymphocytes with IL-4 in the absence of additional costimulators resulted in the increased surface expression of **CD23** (low-affinity Fc epsilon RII), IgM, IL-2R, and MHC class II in a dose-dependent manner. IL-4 alone increased basal levels of proliferation of bulk peripheral blood mononuclear cells but in the presence of Con A inhibited proliferation. In contrast to the activities of IL-4 in the murine system, proliferation of TH1- and TH2-like clones was inhibited in a dose-dependent manner as assessed by antigen-or IL-2-driven in vitro proliferative responses. These observations are consistent with the role of IL-4 as a key player in regulation of both T and B cell responses.

L7 ANSWER 29 OF 67 MEDLINE DUPLICATE 16
95167695 Document Number: 95167695. PubMed ID: 7963531. Effects of

2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on interleukin-4-mediated mechanisms of immunity. Karras J G; Conrad D H; Holsapple M P. (Department of Pharmacology, Medical College of Virginia/Virginia Commonwealth University, Richmond.) TOXICOLOGY LETTERS, (1995 Jan) 75 (1-3) 225-33. Journal code: 7709027. ISSN: 0378-4274. Pub. country: Netherlands. Language: English.

AB Because of similarities in the independent actions of the pleiotropic cytokine, interleukin-4 (IL-4), and the environmental contaminant, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), on murine B-lymphocytes suggested in earlier studies, we have investigated whether the immunosuppression mediated by direct exposure to TCDD in vitro is due to an IL-4-like biological activity. In particular, the ability of TCDD to mimic hallmark responses of B-cells to IL-4, such as upregulation of major histocompatibility complex (MHC) antigens of the class II type, increases in cell surface expression of the low affinity form of the Fc receptor for IgE (**CD23**) and induction of immunoglobulin class switching, was tested. At concentrations that readily suppress B-cell proliferative and **antibody**-forming cell responses, TCDD failed to demonstrate any of the activities of IL-4 observed in parallel cultures. Further, in experiments in which TCDD was preincubated with B-cells before addition of IL-4, no evidence of increased IL-4 activity was observed. Rather, TCDD preincubation resulted in decreased secretion of **IgG1** and IgE in B-cell cultures stimulated to undergo immunoglobulin class switching by incubation with bacterial lipopolysaccharide (LPS) and IL-4. Because TCDD produced comparable suppression of IgM secretion induced by LPS alone (i.e., no IL-4), it appears that TCDD inhibits the formation of fully differentiated B-cells capable of secreting **antibody** and has no effects on class switching events per se. Coupled with previous reports from this and other laboratories, these observations indicate that TCDD is able to suppress secretion of several classes of immunoglobulin.

L7 ANSWER 30 OF 67 MEDLINE DUPLICATE 17

94230956 Document Number: 94230956. PubMed ID: 8176203. **CD23**/IgE-mediated regulation of the specific **antibody** response in vivo. Gustavsson S; Hjulstrom S; Liu T; Heyman B. (Department of Pathology, Uppsala University Hospital, Sweden.) JOURNAL OF IMMUNOLOGY, (1994 May 15) 152 (10) 4793-800. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We have recently reported that IgE Abs specific for TNP are able to enhance the specific IgG response in mice via the low affinity receptor for IgE, Fc epsilon RII, or **CD23**. In this study we show that IgE can up-regulate IgM, **IgG1**, IgG2a, and the IgE response, thereby indicating the possibility of a viscious circle in the maintenance of an allergic response. One of the suggested modes of action of IgE/**CD23** is to increase the ability of B cells to present Ag to T cells. The involvement of T cells in IgE-mediated enhancement of the Ab response was studied in several ways: nude mice were resistant to the effect of IgE and a dramatic effect on the induction of immunologic memory was seen, both by in situ secondary immunizations and in adoptive transfer systems. Basic conditions for the ability of IgE to induce enhancement were established, demonstrating critical importance of factors such as type of Ag and temporal relationship between administration of IgE and Ag. Finally, no evidence for the requirement for **CD23** for a normal (non-IgE induced) Ab response was found, although modulation of the receptor completely abrogated the IgE-induced Ab response.

L7 ANSWER 31 OF 67 SCISEARCH COPYRIGHT 2003 ISI (R)

94:229731 The Genuine Article (R) Number: NG719. ANTIGEN PRESENTATION IS ENHANCED BY TARGETING ANTIGEN TO THE FC-EPSILON-RII BY ANTIGEN-ANTI-FC-EPSILON-RII CONJUGATES. SQUIRE C M; STYLER E J; LEES A; FINKELMAN F D; CONRAD D H (Reprint). VIRGINIA COMMONWEALTH UNIV, DEPT MICROBIOL & IMMUNOL, BOX 980678, MCV STN, RICHMOND, VA, 23298 (Reprint); VIRGINIA COMMONWEALTH UNIV, DEPT MICROBIOL & IMMUNOL, RICHMOND, VA, 23298;

UNIFORMED SERV UNIV HLTH SCI, DEPT MED, BETHESDA, MD, 20814. JOURNAL OF IMMUNOLOGY (01 MAY 1994) Vol. 152, No. 9, pp. 4388-4396. ISSN: 0022-1767. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Targeting Ag to the Fc epsilon RII by Ag-specific IgE has been shown to be an efficient means of enhancing Ag presentation by B cells to Ag-specific T cells. To take advantage of the Fc epsilon RII as a targeting molecule and to investigate whether IgE was required for mediation of the enhanced stimulation, Ag was covalently coupled to anti-Fc epsilon RII by using heterobifunctional crosslinking reagents. These Ag-Ab conjugates were used with T cell lines specific for the Ags, OVA (BB6.5) or rabbit gamma-globulin (CDC35 and D1.6), and splenic B cells to examine both B cell and T cell proliferation in vitro. Significant presentation of Ag-anti-Fc epsilon RII conjugates was apparent at doses of Ag 1,000- to 10,000-fold lower than seen with unconjugated Ag alone. Ag presentation with the use of anti-Fc epsilon RII-Ag conjugates was as good as or better than conjugates with Ab to the adhesion molecule Pgp-1 or control Ab in T cell proliferation and better than those conjugates in B cell proliferation assays (10- to 100-fold). Anti-Fc epsilon RII-Ag conjugates were clearly more effectively presented than Ag-anti-Fc gamma RII conjugates (>100-fold). Mouse Fc epsilon RII is presently known to be expressed on B cells and follicular dendritic cells and these in vitro results suggest that the conjugates would be useful tools for investigating the role of IgE-mediated B cell Ag presentation in vivo. BALB/c mice immunized with OVA-anti-Fc epsilon RII conjugates made a quite significant OVA-specific **IgG1** response and a detectable IgE response. No detectable Ab was produced in response to OVA alone and a minimal response was seen when an isotype-matched control conjugate was used. Thus, the results indicate that Fc epsilon RII targeting is operative both in vivo and in vitro.

L7 ANSWER 32 OF 67 SCISEARCH COPYRIGHT 2003 ISI (R)
94:157756 The Genuine Article (R) Number: NC609. MICE DEFICIENT IN **CD23** REVEAL ITS MODULATORY ROLE IN IGE PRODUCTION BUT NO ROLE IN T-CELL AND B-CELL DEVELOPMENT. STIEF A; TEXIDO G; SANSIG G; EIBEL H; LEGROS G; VANDERPUTTEN H (Reprint). CIBA GEIGY LTD, DEPT BIOTECHNOL, K-681-4-47, CH-4002 BASEL, SWITZERLAND (Reprint); CIBA GEIGY LTD, DEPT BIOTECHNOL, CH-4002 BASEL, SWITZERLAND; CIBA GEIGY LTD, DEPT IMMUNOL, BASEL, SWITZERLAND; UNIV FREIBURG, DEPT RHEUMATOL, FREIBURG, GERMANY. JOURNAL OF IMMUNOLOGY (01 APR 1994) Vol. 152, No. 7, pp. 3378-3390. ISSN: 0022-1767. Pub. country: SWITZERLAND; GERMANY. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB To assess roles of **CD23** in lymphocyte development and immune function in vivo, **CD23**-deficient mice (**CD23**(-/-)) were generated. Mice heterozygous with respect to the defective allele (**CD23**(+/-)) display 50- reduced levels of **CD23** expression on **CD23**(+) cell types. This pattern is consistent with a lack of parental or tissue-specific imprinting of the **CD23** gene. Neither a 50- reduced level nor a complete lack of **CD23** caused profound changes in lymphocyte compartments (thymocytes, peripheral T cells, and B-1 and B-2 B cells). The lack of **CD23** also did not significantly alter in vitro the proliferative response of B cells triggered via the Ag receptor in combination with CD40 ligand, IL-2, and/or IL-4. Effects on polyclonal Ig production were tested in a Th2 cell-driven immune response in vivo after infection with Nippostrongylus brasiliensis, a parasite that dramatically enhances **CD23** expression on B cells. In both primary and secondary immune responses, heterozygous **CD23** (+/-) mice developed slightly higher and **CD23** (-/-) mice similar serum IgE and **IgG1** levels as compared with **CD23** (+/+) wild-type mice. The increase in blood eosinophil counts was similar in all three types of mice. These findings show that after N. brasiliensis infection [a complete lack of **CD23** in vivo neither prohibits nor significantly alters

quantitatively polyclonal IgE levels in serum, and 2) a 50- reduction in cell-surface **CD23** expression (**CD23**(+/-) mice) correlates with slightly increased serum IgE levels.

L7 ANSWER 33 OF 67 MEDLINE

94375866 Document Number: 94375866. PubMed ID: 8089484. Transgene **CD23** expression on lymphoid cells modulates IgE and **IgG1** responses. Texido G; Eibel H; Le Gros G; van der Putten H. (Department of Molecular Cell Biology/Central Nervous System, Ciba-Geigy Limited, Basel, Switzerland.) JOURNAL OF IMMUNOLOGY, (1994 Oct 1) 153 (7) 3028-42. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Transmembrane (m) and soluble (s) forms of **CD23** perform activities related to various immune functions. Abnormal expression patterns of **CD23** on lymphoid cells have been associated with certain pathologic conditions. To explore the effects of **CD23** when it is overexpressed, on lymphoid cell development and immune function in vivo, transgenic mice were generated. These mice overexpressed either mCD23 or a 38-kDa molecular form of sCD23. Transgene expression under the control of Thy-1-regulatory sequences and the mouse Ig heavy chain enhancer (E mu) was prominent in thymus, spleen, bone marrow, and lymph nodes. Cells that expressed the transgenes included most thymocytes, peripheral CD4+ and CD8+ T cells, IgM+/highIgD-/low immature B cells, and IgMlowIgDhigh mature B cells. To resolve the expression pattern in the B cell lineage unambiguously, we used mice that carried a transgene and a disrupted endogenous **CD23** gene simultaneously. Neither mCD23 nor sCD23 overexpression caused significant alterations in lymphoid cell maturation. In addition, basal serum levels of IgE and **IgG1** proved to be normal. In three different experimental immune response paradigms, mCD23 transgenic, but not sCD23 and nontransgenic mice proved to be impaired in increasing serum levels of polyclonal IgE up to expected levels. In addition, mCD23 transgenic mice showed below normal increases of serum **IgG1** levels in two of the three immune responses. In the presence of activated T cells and appropriate lymphokines, B cells from mCD23 mice secreted normal amounts of IgE and **IgG1** in vitro, which suggests that there was no serious impairment of the T-B cell contact required for Ig production. In addition, there is no evidence for a significant role of mCD23 in IgE clearance. Therefore, we discuss alternative mechanisms by which mCD23+ B and/or T cells influence Ig production.

L7 ANSWER 34 OF 67 MEDLINE DUPLICATE 18

95053710 Document Number: 95053710. PubMed ID: 7964461. Evidence for an interleukin 4-inducible immunoglobulin E uptake and transport mechanism in the intestine. Ramaswamy K; Hakimi J; Bell R G. (J.A. Baker Institute for Animal Health, College of Veterinary Medicine, Cornell University, Ithaca, New York 14853.) JOURNAL OF EXPERIMENTAL MEDICINE, (1994 Nov 1) 180 (5) 1793-803. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB Immunoglobulin (Ig) E is the principal Ig involved in immediate hypersensitivities and chronic allergic diseases such as asthma. Helminths are the most potent infectious agents known for their capacity to stimulate IgE production during the course of infection. In rats, the nematode Trichinella spiralis typically elicits a strong parasite-specific IgE response during infection, and this IgE **antibody** has been shown to be protective against the parasite in passive transfer experiments. The study reported here analyzed the fate of 125I-labeled myeloma IgE (IR162) in normal and T. spiralis-infected rats after intravenous injection. T. spiralis infection induced a capacity for specific binding to the gut wall of 125I-IgE rather than 125I-**IgG1**, as well as the transport of IgE, but not **IgG1**, into the gut lumen. Peak intestinal uptake and transport of 125I-IgE occurred during the first and second weeks after injection but was not elevated in the

fourth week, that is, after intestinal adult worms had been expelled. Neither 125I-IgE uptake in the gut wall nor transport to the lumen could be ascribed to tissue damage or vascular leakage. Luminal transport occurred in the small intestine and not the liver, which only transports low molecular weight degraded 125I-IgE. Calculations based on the amount of intact IgE in the lumen suggest that, in a 24-h period, up to 20% of injected 125I-IgE can be transported to the gut lumen during the peak transport period, between 6 and 14 d after infection. The intestinal IgE binding and transport response can be adoptively transferred with T. spiralis immune CD4+ OX22- (CD45RC-) lymphocytes, which are protective, but not the nonprotective sister population CD4+ OX22+ (CD45RC+) of lymphocytes isolated simultaneously from thoracic duct lymph of infected rats. The intravenous infusion of recombinant rat interleukin 4 also elicited significant intestinal uptake of 125I-IgE. We also present evidence for the presence of **CD23** on rat intraepithelial lymphocytes. These data provide evidence for a novel, inducible, intestine-specific IgE uptake and transport mechanism.

L7 ANSWER 35 OF 67 MEDLINE DUPLICATE 19
94237219 Document Number: 94237219. PubMed ID: 7514131. T cell subset distribution and B cell hyperreactivity in mice expressing interleukin-4 under the control of major histocompatibility complex class I regulatory sequences. Erb K J; Holtschke T; Muth K; Horak I; Schimpl A. (Institut fur Virologie and Immunbiologie, Universitat Wurzburg, Germany.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1994 May) 24 (5) 1143-7. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Transgenic mice in which interleukin-4 (IL-4) is expressed under the control of the major histocompatibility complex (MHC) class I regulatory sequences show low level expression of IL-4 in all organs investigated. Several weeks after birth the animals develop thymus hypoplasia with a loss of CD4+CD8+ double-positive cells and a relative increase in the mature population, especially, and in contrast to previously published lines, the CD4+ single-positive cells. In the periphery, T lymphocytes eventually decline, CD8+ cells being more strongly affected. Many of the residual T cells exhibit the CD44highMel-14low phenotype of antigenically experienced T cells. B cells also show an activated phenotype with respect to size, MHC class II and **CD23** expression, are more readily stimulated by anti-mu F(ab')2 **antibodies** than are B cells from control littermates, and show a higher spontaneous and antigen-induced production of **IgG1** and IgE.

L7 ANSWER 36 OF 67 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. DUPLICATE 20
94072760 EMBASE Document No.: 1994072760. Identification of a T cell membrane protein possibly involved in IL-4- induced B cell immunoglobulin class switching to IgE. Matsushita S.; Katz D.H.. Division of Immunology, Medical Biology Institute, 11077 North Torrey Pines Road,San Diego, CA 92037, United States. Cellular Immunology 153/2 (378-391) 1994. ISSN: 0008-8749. CODEN: CLIMB8. Pub. Country: United States. Language: English. Summary Language: English.

AB The murine T cell hybridoma line, MBI-1.15, secretes a 17-kDa protein which decreases binding activity of the **CD23** molecule for its natural ligand, IgE. This protein, denoted .epsilon. receptor-modulating protein (.epsilon.RMP), was previously characterized and shown to be a novel serine protease. The present studies show that, in addition to modulating **CD23**, .epsilon.RMP costimulates with IL-4 the de novo synthesis and secretion of IgE and **IgG1** by cultured B cells. Since such costimulating activity is reminiscent of a similar synergism with IL-4 previously observed with cell membranes from activated T cells, we examined isolated membranes from the .epsilon.RMP-producing MBI-1.15 T cell line for comparable activity; indeed, as shown herein, MBI-1.15 cell membranes do exhibit this synergism. Furthermore, we show that a monoclonal **antibody** (mAb), 2E5B, specific for the 17-kDa soluble

form of .epsilon.RMP, blocks the costimulating activities of both the soluble .epsilon.RMP and MBI-1.15 T cell membranes for IL-4-induced de novo synthesis of IgE by cultured B cells. This anti-.epsilon.RMP mAb also detects a 36-kDa membrane-bound protein species which appears to be related to soluble .epsilon.RMP by immunochemical criteria. The membrane-bound proteins, present on MBI-1.15 T cells, induce germ-line IgE heavy chain transcripts (I.epsilon.) in I-29 B cells independently of IL-4, and this inductive event is also specifically blocked by the 2E5B anti-.epsilon.RMP mAb. These findings suggest that T cell membrane-bound .epsilon.RMP molecules are crucial proteins involved in contact-dependent B cell class switching in the course of IgE biosynthesis. Finally, both IL-4 and .epsilon.RMP induce I.epsilon. on I-29 B cells, but neither molecule by itself can induce class switching to IgE synthesis by splenic B cells. This clearly suggests that both .epsilon.RMP and IL-4 have another important molecular effect (which may or may not be identical) on B cells, that is essential for class switching, but only when both molecules are present simultaneously is the complete mechanism of class switching manifested.

L7 ANSWER 37 OF 67 MEDLINE

94302468 Document Number: 94302468. PubMed ID: 8029636. Prolonged in vivo IL-4 treatment inhibits antigen-specific **IgG1** and IgE formation. van Ommen R; Vredendaal A E; Savelkoul H F. (Department of Immunology, Erasmus University, Rotterdam, The Netherlands.) SCANDINAVIAN JOURNAL OF IMMUNOLOGY, (1994 Jul) 40 (1) 1-9. Journal code: 0323767. ISSN: 0300-9475. Pub. country: ENGLAND: United Kingdom. Language: English.

AB IL-4 is obligatory for primary IgE responses, whereas primary **IgG1** and secondary IgE responses are partially IL-4 independent. To investigate the effect of IL-4 on the antigen-specific memory formation for these isotypes, BALB/c mice were treated after primary TNP-KLH immunization with recombinant IL-4 for a period fo 4 months. This prolonged presence of a high IL-4 level resulted in increased serum levels of total **IgG1** and IgE, whereas total IgG2a did not change. The expression of **CD23**, but not I-Ad, increased on the splenic B cells. IL-4 treatment did not affect the IL-4 production by Con A stimulated spleen cells, whereas it did decrease the IFN-gamma production. In the same mice the TNP-specific **IgG1** and IgE serum levels, however, were decreased. Similar results were found when the antigen was continuously present during the IL-4 treatment. Furthermore, it was shown that IL-4 decreased the formation of **IgG1** and IgE memory cells. These results point to different effects of IL-4 in regulating antigen-specific and bystander responses.

L7 ANSWER 38 OF 67 CAPLUS COPYRIGHT 2003 ACS

1993:493523 Document No. 119:93523 Murine and human cytokine (CD40-L) which binds to CD40, and soluble CD40 and CD40 fusion molecules. Armitage, Richard J.; Fanslow, William C.; Spriggs, Melanie K. (Immunex Corp., USA). PCT Int. Appl. WO 9308207 A1 19930429, 79 pp. DESIGNATED STATES: W: AU, CA, FI, JP, KR, NO; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US8990 19921023. PRIORITY: US 1991-783707 19911025; US 1991-805723 19911205.

AB The title CD40-L mols. are disclosed, as are related DNA sequences, vectors, and transformed host cells. The murine and human CD40-L polypeptides bind to the extracellular binding region of a CD40 receptor. Also provided are a CD40/**IgG1** Fc region fusion protein and a sol. CD40 protein (sCD40) comprising the extracellular portion of CD40; both the CD40/Fc and sCD40 can inhibit CD40-L or anti-CD40 monoclonal **antibody**-induced B-cell stimulation, interleukin-4-induced IgE stimulation, and interleukin-4-induced **CD23** induction in B-cells. Construction is described of a CD40/Fc DNA for prodn. of a fusion protein for use in detecting cDNA clones encoding a CD40 ligand. Also described are selection of a cell line putatively expressing CD40-L, prepn. of a cDNA library for expression cloning of murine CD40-L,

cross-species hybridization methodol. used to isolate a human CD40-L homolog, anti-allergy therapeutic effects of sCD40 and CD40/Fc fusion protein, etc. Interaction of CD40 with its ligand was evidently the principal mol. interaction responsible for T-cell contact-dependent induction of B-cell growth and differentiation to both antigen-specific **antibody** prodn. and polyclonal Ig secretion.

L7 ANSWER 39 OF 67 CAPLUS COPYRIGHT 2003 ACS
1993:232271 Document No. 118:232271 T-cell proteins for B-cell Ig class switching and IgE binding modulation. Katz, David H.; Matsushita, Sho (Medical Biology Institute, USA). PCT Int. Appl. WO 9302696 A1 19930218, 75 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US6553 19920806. PRIORITY: US 1991-741671 19910807.

AB A crude protein prepn. known as suppressive factor of allergy (SFA) consists of 2 functionally and biochem. distinct proteins: (1) a 30-kDa protein which suppresses IgE biosynthesis and is distinct from .gamma.-interferon, and (2) a sol. .epsilon. receptor-modulating protein (.epsilon.RMP) of mol. wt. 17 kDa which modulates **CD23**, induces germline IgE heavy chain transcripts, and enhances IgE biosynthesis by B-cells in the presence of interleukin 4. .epsilon.RMP is a serine proteinase, decreases the avidity of binding of IgE to the **CD23** low-affinity IgE Fc receptor on B-cells without decreasing the quant. expression of **CD23**, requires CD4+ T-cells to mediate its effect on B-cells, and has a unique partial internal sequence Ala-Lys-Pro-Ala-Pro-Lys-Lys-Glu-Glu-Lys-Lys-Lys-Lys-Ala-Ala-Ala-Lys-Lys. .epsilon.RMP also exists in a 36-kDa T-cell membrane form. Both forms are useful in diagnostic assays and for therapeutically altering the immune response in mammals. A murine T-cell hybridoma which produces high titers of .epsilon.RMP is described.

L7 ANSWER 40 OF 67 SCISEARCH COPYRIGHT 2003 ISI (R)
94:3142 The Genuine Article (R) Number: MM689. SWITCHING CAPACITY OF FC-EPSILON-RII-POSITIVE AND FC-EPSILON-RII-NEGATIVE MURINE B-CELLS. FOY T M; WALDSCHMIDT T J (Reprint). UNIV IOWA, COLL MED, DEPT PATHOL, IOWA CITY, IA, 52242 (Reprint); UNIV IOWA, COLL MED, DEPT PATHOL, IOWA CITY, IA, 52242. EUROPEAN JOURNAL OF IMMUNOLOGY (DEC 1993) Vol. 23, No. 12, pp. 3208-3216. ISSN: 0014-2980. Pub. country: USA. Language: ENGLISH. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB In previous studies, our laboratory demonstrated the utility of the low affinity IgE Fc receptor (FcepsilonRII) in delineating a number of murine B cell subsets. In the spleen, the FcepsilonRII is expressed on mature conventional B cells but is absent on marginal zone B cells. In the peritoneal cavity, the receptor is present on all conventional B cells, but is not expressed on fresh peritoneal Ly1/sister B cells. The studies in this report compared the ability of these B cell poputations to isotype switch. Using a lipopolysaccharide (LPS)- and interleukin (IL)-4-driven system, sort-purified FcepsilonRII- positive and -negative B cells from peritoneum and spleen were tested for switching to **IgG1**, IgE, and IgA. The results demonstrated that regardless of their source, FcepsilonRII+ B cells produced significant levels of **IgG1** and IgE. Similar results were obtained with FcepsilonRII- (marginal zone) B cells obtained from spleen. In contrast, FcepsilonRII- (Ly1/sister) peritoneal B cells were found to produce **IgG1** and IgA, but were incapable, of secreting significant levels of IgE. Further studies tested for LPS and IL-4-induced expression of FcepsilonRII and Thy1 on the various B cell populations. These experiments demonstrated the induction of the FcepsilonRII on all B cells, regardless of their initial resting levels. Additionally, Thy1 was found to be induced only on those B cell subsets capable of producing IgE. Taken together, the results demonstrate a correlation between IgE secretion and Thy1 expression, and no apparent correlation between the presence of the FcepsilonRII and isotype commitment.

L7 ANSWER 41 OF 67 SCISEARCH COPYRIGHT 2003 ISI (R)
93:324702 The Genuine Article (R) Number: LC381. ENGAGEMENT OF CD40 LOWERS THE THRESHOLD FOR ACTIVATION OF RESTING B-CELLS VIA ANTIGEN RECEPTOR. WHEELER K (Reprint); POUND J D; GORDON J; JEFFERIS R. UNIV BIRMINGHAM SCH MED, DEPT IMMUNOL, BIRMINGHAM B15 2TT, ENGLAND (Reprint). EUROPEAN JOURNAL OF IMMUNOLOGY (MAY 1993) Vol. 23, No. 5, pp. 1165-1168. ISSN: 0014-2980. Pub. country: ENGLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Cross-linking of surface Ig (sIg) on resting B cells can generate intracellular signals; however, for T-dependent antigens to promote growth and differentiation additional surface receptors must be engaged. Ligation of CD40 can stimulate B cell proliferation in the presence of interleukin-4. A recently identified counterstructure for CD40 is found on T helper cells and is believed to represent the cognate ligand for B cell activation. This study investigates the role of CD40 as an accessory molecule in sIg-dependent B cell activation. Simultaneous ligation of sIg and CD40 by monoclonal **antibodies** (mAb) in the presence of mouse L cells which express human Fcgamma receptor type II (FcgammaRII-L cells) results in potent stimulation of small resting B cells. When CD40 is co-ligated, picomolar concentrations of mouse **IgG1** anti-mu, and anti-delta mAb can stimulate B cell proliferation. This requires interaction of the anti-Ig mAb with the FcgammaRII-L cells: a mouse IgG2a anti-mu mAb which is not recognized by FcgammaRII, was greater-than-or-equal-to 1000-fold less effective. These findings suggest a mechanism for B cell activation whereby engagement of T cells via CD40 and its cognate ligand provides potent enhancement of signals delivered through sIg. Based on these observations, models for the activation of B cells by T-dependent antigens are presented.

L7 ANSWER 42 OF 67 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
93102347 EMBASE Document No.: 1993102347. Biphasic effect of kallikrein on IgE and **IgG1** syntheses by LPS/IL-4-stimulated B cells.
Matsushita S.; Katz D.H.. Division of Immunology, Medical Biology Institute, 11077 North Torrey Pines Road,La Jolla, CA 92037, United States. Cellular Immunology 146/1 (210-214) 1993.
ISSN: 0008-8749. CODEN: CLIMB8. Pub. Country: United States. Language: English. Summary Language: English.

AB .epsilon. receptor modulating protein (.epsilon.RMP) was identified and purified in our previous studies as a murine T cell-derived soluble 17-kDa chymotryptic serine protease which suppresses avidity of binding between IgE and **CD23** (low affinity Fc receptor for IgE) without decreasing the quantitative expression of the **CD23** molecule. Some, but not all, of the other known soluble serine proteases showed .epsilon.RMP-like **CD23**-modulating activities. Further studies indicated that .epsilon.RMP exists not only as a soluble protein but also as a 36-kDa T-cell surface form. Both soluble and membrane bound .epsilon.RMP can induce purified splenic B cells to secrete IgE in the presence of IL-4 even without lipopolysaccharide (LPS). In this study, therefore, we have tested effects of several known serine proteases on Ig production in vitro and have found that: (i) coculture of splenic B cells in the presence of LPS and IL-4 with serine proteases which have .epsilon.RMP-like substrate specificity, such as ein and .alpha.-chymotrypsin, results in a significant increase of **IgG1** and a slight increase of IgE secretion at low concentrations, and significant suppression at high concentrations in an isotype-selective manner; and (ii) the effects of these proteases are blocked by phenylmethylsulfonyl fluoride but not by indomethacin, suggesting that serine protease activity but not prostaglandin E2 is involved. The biological significance of the possible involvement of serine proteases on Ig class switching is discussed.

L7 ANSWER 43 OF 67 MEDLINE DUPLICATE 21

94011854 Document Number: 94011854. PubMed ID: 8407286. Effect of immunological stimulation on the production of platelet-activating factor by rat peritoneal cells: its relevance to anaphylactic reactions. Pellon M I; Fernandez-Gallardo S; Gijon M A; Garcia M C; Liu F T; Sanchez Crespo M. (Departamento de Bioquimica y Fisiologia-CSIC, Facultad de Medicina, Valladolid, Spain.) IMMUNOPHARMACOLOGY, (1993 Jul-Aug) 26 (1) 73-82. Journal code: 7902474. ISSN: 0162-3109. Pub. country: Netherlands. Language: English.

AB The production of platelet-activating factor (PAF) by rat peritoneal cells was studied using as stimuli either monoclonal IgE, **IgG1** or IgG2b anti-DNP (2,4-dinitrophenyl), and DNP-BSA. Peritoneal cells sensitized in vitro with any of these **antibodies** at concentrations higher than 10 nM and challenged with 1 microM DNP-BSA produced PAF. PAF production was also elicited by preformed IgE/ and IgG2b/DNP-BSA immune complexes, preferentially at a large antigen/ **antibody** ratio. The production of PAF was unrelated to the activation of mast cells, since it occurred in populations depleted of mast cells by adherence to plastic dishes. Moreover, the release of [3H]serotonin from IgE-sensitized mast cells showed a time-course more rapid than PAF production and occurred in cells sensitized with IgE at concentrations lower than those required for PAF formation. In contrast, peritoneal cells sensitized with **IgG1** and IgG2b failed to release [3H]serotonin. Rat peritoneal cells showed a significant ability to catabolize PAF by intracellular PAF-acetylhydrolase in view of both the amounts of enzyme activity assayed in cellular homogenates, and the 15-fold increase on controls of PAF quantities detected in peritoneal cells treated with phenylmethylsulfonyl fluoride (PMSF), a known inhibitor of PAF-acetylhydrolase. The PAF activity produced upon PMSF addition showed a retention time on reverse-phase HPLC which suggests structural identity to PAF produced by either immunological challenge or ionophore A23187. These data suggest that PAF formed during rat passive anaphylaxis reactions depends on the activation of mononuclear phagocytes. This production may be triggered by two types of low affinity receptors: Fc epsilon RII/**CD23** and Fc gamma R. The ability of peritoneal cells to catabolize PAF by intracellular acetylhydrolase seems unaffected by immunological stimulation.

L7 ANSWER 44 OF 67 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 22

93036024 EMBASE Document No.: 1993036024. The detection of autoantibodies to IgE in plasma of individuals infected with hookworm (Necator americanus) and the demonstration of a predominant **IgG1** anti-IgE autoantibody response. Shakib F.; Pritchard D.I.; Walsh E.A.; Smith S.J.; Powell-Richards A.; Kumar S.; Edmonds P.. Deprtment of Immunology, University Hospital, Queen's Medical Centre,Nottingham NG7 2UH, United Kingdom. Parasite Immunology 15/1 (47-53) 1993. ISSN: 0141-9838. CODEN: PAIMD8. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB In this study we have demonstrated significantly elevated levels of circulating IgG autoanti-IgE **antibody** in hookworm infected individuals from Kebasob village on Karbar Island, Papua New Guinea. Although anti-IgE activity was demonstrable in **IgG1**, IgG3 and IgG4, **IgG1** was by far the most important subclass of IgG anti-IgE in terms of frequency of detection (34/39; 87.2%) and magnitude of increase (P = 0.0000); with IgG3 (16/39; 41.0%) and IgG4 (15/39; 38.5%) **antibodies** being considerably less prevalent. Plasma levels of **IgG1** anti-IgE (P = 0.0019) and IgG3 anti-IgE (P = 0.0034) showed significant correlations with total IgE concentrations, but not with IgE specific to excretory-secretory worm products; thus suggesting that anti-IgE synthesis is more related to polyclonal hyper IgE production than to antigen-specific IgE stimulation. No correlation was seen between IgG subclass anti-IgE levels and faecal egg counts or worm burden. Given that our data failed to show a negative or a positive correlation between anti-IgE and the degree of infection with hookworm, it is tempting to

speculate that the main role of autoanti-IgE is to provide the host with protection against immune complex- and IgE-mediated hypersensitivity reactions to parasitic antigens.

L7 ANSWER 45 OF 67 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
93008084 EMBASE Document No.: 1993008084. Immunoglobulin D (IgD)-deficient mice reveal an auxiliary receptor function for IgD in antigen-mediated recruitment of B cells. Roes J.; Rajewsky K.. Institute for Genetics, University of Cologne, Weyertal 121,D-5000 Koln 41, Germany. Journal of Experimental Medicine 177/1 (45-55) 1993.
ISSN: 0022-1007. CODEN: JEMEAV. Pub. Country: United States. Language: English. Summary Language: English.
AB To assess the role of immunoglobulin D (IgD) in vivo we generated IgD-deficient mice by gene targeting and studied B cell development and function in the absence of IgD expression. In the mutant animals, conventional and CD5-positive (B1) B cells are present in normal numbers, and the expression of the surface markers CD22 and **CD23** in the compartment of conventional B cells indicates acquisition of a mature phenotype. As in wild-type animals, most of the peripheral B cells are resting cells. The IgD-deficient mice respond well to T cell-independent and -dependent antigens. However, in heterozygous mutant animals, B cells expressing the wild type IgH locus are overrepresented in the peripheral B cell pool, and T cell-dependent **IgG1** responses are further dominated by B cells expressing the wild-type allele. Similarly, in homozygous mutant (IgD-deficient) animals, affinity maturation is delayed in the early primary response compared to control animals, although the mutants are capable of generating high affinity B cell memory. Thus, rather than being involved in major regulatory processes as had been suggested, IgD seems to function as an antigen receptor optimized for efficient recruitment of B cells into antigen-driven responses. The IgD-mediated acceleration of affinity maturation in the early phase of the T cell-dependent primary response may confer to the animal a critical advantage in the defense against pathogens.

L7 ANSWER 46 OF 67 MEDLINE DUPLICATE 23
93172603 Document Number: 93172603. PubMed ID: 8382322. Suppression of IgE production by IPD-1151T (suplatast tosilate), a new dimethylsulfonium agent: (1). Regulation of murine IgE response. Yanagihara Y; Kiniwa M; Ikizawa K; Yamaya H; Shida T; Matsuura N; Koda A. (Clinical Research Center for Allergy, National Sagamihara Hospital, Kanagawa, Japan.) JAPANESE JOURNAL OF PHARMACOLOGY, (1993 Jan) 61 (1) 23-30. Journal code: 2983305R. ISSN: 0021-5198. Pub. country: Japan. Language: English.
AB The effect of IPD-1151T, a new dimethylsulfonium compound, on the IgE response was investigated in the mouse system. The oral administration of IPD-1151T to immunized BALB/c mice suppressed the primary IgE **antibody** response and depressed the elevation of serum IgE levels, whereas the same treatment did not affect the IgG **antibody** response. The enhanced expression of low-affinity IgE receptor (Fc epsilon RII/**CD23**) on the spleen cells of immunized mice was also inhibited by IPD-1151T administration. It was further demonstrated from the adoptive transfer experiment that IPD-1151T, administered to hapten-primed B cell donors, but not to carrier-primed T cell donors, exerted its suppressive influence on the hapten-specific secondary IgE **antibody** response in irradiated syngeneic recipients. Interestingly, IPD-1151T concentration-dependently inhibited the production of interleukin 4 (IL-4) by D10G4.1, known to be a typical Th2 clone. However, IPD-1151T did not suppress the production of IgE and **IgG1** by normal splenic B cells stimulated with lipopolysaccharide and IL-4. Moreover, IL-4-induced expression of Fc epsilon RII on normal spleen cells was not inhibited by the agent. These results strongly suggest that the IgE-suppressive activity of IPD-1151T is most likely due to the inhibition of IL-4 production at the T cell level.

L7 ANSWER 47 OF 67 MEDLINE
93318718 Document Number: 93318718. PubMed ID: 7687088. A study of the interrelationship between circulating IgG subclass anti-IgE autoantibodies, IgE and soluble **CD23** in asthma. Shakib F; Boulstridge L; Smith S J. (Department of Immunology, University Hospital, Queen's Medical Centre, Nottingham, U.K.) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1993 Jan-Feb) 21 (1) 29-4. Journal code: 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.

AB In this paper we hypothesise that circulating autoanti-IgE **antibodies**, which are found in allergic asthma patients, could potentially enhance IgE synthesis by blocking its binding to **CD23** on B lymphocytes, thereby potentiating the release of soluble fragments of **CD23** which have B cell growth-promoting activity. We have investigated this possibility indirectly by measuring soluble (s) **CD23** and IgG subclass anti-IgE **antibody** levels in asthmatic patients' sera, to find out if the two parameters are related. However, we were unable to show any significant correlations between serum IgG subclass anti-IgE activities and sCD23 levels. This may have been due, at least in part, to the heterogeneous epitope specificity of the autoanti-IgE being detected. Interestingly, there was a significant inverse correlation ($p = 0.0178$) between serum IgE and sCD23 levels in asthma; an observation which underlines the notion that binding of IgE to membrane **CD23** abrogates the release of sCD23. The present study confirms and extends previous reports of significantly raised circulating levels of IgG anti-IgE in asthma patients ($p = 0.0004$), by further demonstrating that IgG anti-IgE is mostly restricted to **IgG1**. Given that **IgG1** binds very efficiently to C1q and Fc gamma Rs, our observation lends further support to the notion that IgG anti-IgE may facilitate the removal of IgE-allergen complexes by triggering IgG effector function pathways.

L7 ANSWER 48 OF 67 MEDLINE DUPLICATE 24
92291505 Document Number: 92291505. PubMed ID: 1318334. B cell activator. Effects on B cell expression of **CD23**, proliferation, and **antibody** secretion. Marcelletti J F; Matsushita S; Katz D H. (Division of Immunology, Medical Biology Institute, La Jolla, CA 92037.) JOURNAL OF IMMUNOLOGY, (1992 Jun 15) 148 (12) 3857-63. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The studies herein describe a B cell hybridoma-derived, low m.w. (less than 1000 Da), hydrophilic mediator denoted B cell activator (BCA). BCA stimulates B cell expression of IgE-specific FcR (Fc epsilon RII or **CD23**) in a manner similar to IL-4. However, BCA can be readily distinguished from IL-4 because it does not 1) enhance B cell Ia expression; 2) bind 11B11 anti-IL-4 mAb; or 3) elicit superinduction of Fc epsilon RII expression or IgE production in cultures of LPS-activated B cells. Moreover, BCA is considerably more mitogenic than IL-4 for LPS-activated B cells and, in contrast to IL-4, lacks mitogenicity for anti-mu-activated B cells. BCA can enhance IgG2b and IgG3 production by LPS-activated B cells, responses that are suppressed by IL-4. BCA alone did not stimulate IgE and **IgG1** production by LPS-activated B cells, but exerted synergistic activity when combined with IL-4 in stimulating secretion of these **antibody** isotypes. Finally, secondary Ag-driven **IgG1**, IgE, and IgA **antibody** responses can be stimulated by BCA in vitro. Thus, BCA appears to be a novel mediator with broad B cell activation properties.

L7 ANSWER 49 OF 67 MEDLINE DUPLICATE 25
93017913 Document Number: 93017913. PubMed ID: 1329399. Prostaglandin E2 and cAMP inhibit B lymphocyte activation and simultaneously promote IgE and **IgG1** synthesis. Roper R L; Phipps R P. (Immunology and Immunotherapy Division, Cancer Center, University of Rochester, School of Medicine and Dentistry, NY 14642.) JOURNAL OF IMMUNOLOGY, (1992 Nov 1) 149 (9) 2994-91. Journal code: 2985117R. ISSN: 0022-1767. Pub. country:

United States. Language: English.

AB Macrophage-secreted prostaglandins of the E series inhibit numerous immunologic events, including IgM secretion by B lymphocytes. In this study, we investigated whether PGE also regulates the activation of normal quiescent murine B cells and subsequent isotype differentiation to IgE and **IgG1** production. PGE2 and PGE1 were found to inhibit cellular enlargement induced by IL-4 or bacterial LPS, IL-4 and LPS, or anti-mu and IL-4 by approximately 75%, and completely inhibit enlargement in response to anti-mu **antibody**. PGE2 also suppresses activation-induced class II MHC up-regulation by 35% and expression of the low affinity IgE receptor, Fc epsilon RII/**CD23**, by 30%. Interestingly, PGE completely inhibits a fraction of cells from these activation events, while other cells fully respond to activation stimuli, even in the presence of high PGE2 concentrations. Therefore, a PGE-resistant subset of B lymphocytes may exist. A closely related PG, PGF2 alpha, had no immunoregulatory effect in these systems. Because PGE induces production of cAMP in B cells, we determined whether other agents that increase cAMP could inhibit B cell activation. Cholera toxin and dibutyryl cAMP mimicked the ability of PGE2 to inhibit B cell enlargement, and class II MHC and Fc epsilon RII induction, suggesting that PGE2 signaling occurs via cAMP. In addition, cholera toxin and dibutyryl cAMP inhibited B cell activation much more potently (90-100% inhibition) than PGE, indicating that whereas all B cells are cAMP-sensitive only some are PGE-sensitive. Although PGE inhibits activation-associated events, we previously reported that PGE enhances IL-4 and LPS-induced differentiation to IgE and **IgG1** synthesis. To investigate the relationship between the cells that are activation-inhibited and those that are differentiation-enhanced by PGE, we sorted B cell subsets by FACS and determined their relative abilities to produce IgM, **IgG1**, and IgE in response to IL-4 and LPS in the presence of PGE. The population of lymphocytes that was unaffected by PGE in terms of class II hyperexpression was also unaffected by PGE for Ig synthesis, again indicating a PGE-resistant subpopulation of B cells. Furthermore, the PGE activation-inhibited subset of B cells was responsive to PGE enhancement of IL-4-induced class switching, reducing IgM synthesis and inducing a sevenfold increase in IgE and **IgG1** synthesis compared with other sort groups. These results are consistent with the hypothesis that the B lymphocytes that are PGE activation-inhibited are the same cells that are PGE differentiation-enhanced.(ABSTRACT TRUNCATED AT 400 WORDS)

L7 ANSWER 50 OF 67 MEDLINE DUPLICATE 26

92347407 Document Number: 92347407. PubMed ID: 1386315. Co-crosslinking Fc epsilon RII/**CD23** and B cell surface immunoglobulin modulates B cell activation. Campbell K A; Lees A; Finkelman F D; Conrad D H. (Department of Microbiology and Immunology, Virginia Commonwealth University, Richmond.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1992 Aug) 22 (8) 2107-12. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Previous studies have shown that a highly multivalent from of anti-IgD or anti-IgM, prepared by conjugating the respective **antibodies** to dextran, causes extensive B cell proliferation with ng/ml concentrations of the anti-immunoglobulin (Ig). A modification of this system has been exploited to investigate the effect of co-crosslinking the Fc epsilon RII and surface Ig by binding DNP to the dextran backbone (DNP-dextran) and employing a DNP-specific monoclonal IgE of either rat or mouse origin. Addition of anti-IgD- H delta a/1 [DNP-dextran] or anti-IgM-[DNP-dextran] to purified, resting murine B cells resulted in B cell proliferation over a broad dose (0.03-30 micrograms/ml). Addition of DNP-specific rat or mouse IgE dramatically modulated the proliferative response. Proliferation in response to doses greater than 0.3 microgram/ml H delta a/1-[DNP-dextran] was consistently reduced in a dose-dependent manner in the presence of increasing amounts of IgE while proliferation to lower concentrations of H delta a/1-[DNP-dextran] was slightly enhanced or not

influenced at all by the IgE anti-DNP. Interleukin-4 (IL-4) significantly increased the IgE effect, in line with its known enhancing effects on Fc epsilon RII levels. Experiments measuring Ig production rather than proliferation demonstrated that in the presence of IgE anti-DNP, B cells produced lower amounts of immunoglobulin (**IgG1** or IgM) in response to an anti-Ig signal. Control experiments demonstrated that the IgE effect on proliferation was blocked by monoclonal anti-Fc epsilon RII, but not anti-Fc gamma RII, thus demonstrating the necessity for IgE/Fc epsilon RII interaction. In addition, the necessity for co-crosslinking was shown by the inability of IgE anti-DNP to affect the proliferative response to H delta a/l-dextran even in the presence of various doses of DNP-dextran. These results demonstrate that co-crosslinking of sIg and the Fc epsilon RII results in an altered B cell response to anti-Ig mediated activation. IL-4 does not ablate this inhibition, in contrast to the effect of co-crosslinking Fc gamma RII and surface Ig, suggesting a model whereby IgE can modulate its own production.

L7 ANSWER 51 OF 67 MEDLINE DUPLICATE 27
92347402 Document Number: 92347402. PubMed ID: 1379186. Identification of a source of biologically active CD40 ligand. Armitage R J; Sato T A; Macduff B M; Clifford K N; Alpert A R; Smith C A; Fanslow W C. (Department of Immunology, Immunex Research and Development Corporation, Seattle, WA 98101.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1992 Aug) 22 (8) 2071-6. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB We have identified the murine thymoma line EL4 as a source of biologically active CD40 ligand. Using a biotin-labeled soluble CD40.Fc fusion protein, consisting of the extracellular domain of human CD40 and the Fc region of human **IgG1**, EL4 cells were subjected to repeated flow cytometric cell sorting to select for cells with enhanced biotinylated CD40.Fc binding. After nine rounds of sorting, the number of CD40.Fc binding sites/cell had risen from 450 on the unsorted parental EL4 cells to 15,000 on EL40.9 cells (EL4 cells sorted with biotinylated CD40.Fc for nine rounds). Scatchard analysis of radiolabeled CD40.Fc binding revealed that the surface-expressed CD40 ligand on parental EL4 and EL40.9 cells bound its receptor with a single class of high-affinity sites (Kd = 0.5 nM). Supernatant (SN) from the sorted EL40.9 cells was found to contain human and murine B cell stimulatory activity which could be removed by preclearing with immobilized CD40.Fc, confirming the presence of soluble CD40 ligand in the preparations. EL40.9 supernatant enhanced soluble **CD23** (sCD23) release and induced IgE secretion from interleukin 4-stimulated human B cells. In addition, EL40.9 SN contained proliferative activity for anti-IgM-activated murine B cells which could be removed by treatment with immobilized CD40.Fc. However, the same SN had no demonstrable activity on the proliferation of human B cells. The results presented here describe, for the first time, a source of membrane-bound and soluble CD40 ligand. The soluble form of this murine ligand has activity on murine and human B cells and induces some of the functional responses predicted for the ligand based on the action of stimulatory **antibodies** directed against the human CD40 surface molecule.

L7 ANSWER 52 OF 67 MEDLINE DUPLICATE 28
92395174 Document Number: 92395174. PubMed ID: 1326002. Control of human B cell tumor growth in severe combined immunodeficiency mice by monoclonal anti-B cell **antibodies**. Durandy A; Brousse N; Rozenberg F; De Saint Basile G; Fischer A M; Fischer A. (Institut National de la Sante et de la Recherche Medicale, U 132, Hopital des Enfants-Malades, Paris, France.) JOURNAL OF CLINICAL INVESTIGATION, (1992 Sep) 90 (3) 945-50. Journal code: 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB Severe combined immunodeficiency (scid) mice develop EBV + B cell tumors after infusion of EBV + B cells or of B cells and EBV. In this study, scid mice were infused with B cell lines derived from three patients who

developed a B lymphocyte proliferative disorder after bone marrow or organ transplantation. Intraperitoneal injection of 5 x 10(6) B cells induced tumor growth in all mice, leading to death within 60 d. Human B cells were identified in spleen and bone marrow by means of immunofluorescence or EBV genome amplification, and human IgM was detected in serum. Infusion of murine monoclonal **antibodies** specific for human B cell membrane antigens CD21, CD24, and **CD23** was effective in 80- of animals, against two of the three cell lines preventing tumor development or inducing remission according to the time of treatment. The effect was **antibody** dose dependent and was optimal with four intravenous infusions of at least 0.1 mg 4 d apart. Human IgM in serum and human B cells in spleen and bone marrow became undetectable when peritoneal tumors regressed completely. Infusions of **IgG1** isotype-matched anti-CD4 **antibody** or anti-CD3 **antibody** had no effect. Tumors developed or recurred in 50- of these animals injected with one of the B cell line 3 mo after treatment was stopped. The same anti-CD21 and anti-CD24 **antibodies** had been used to treat the three patients, and shown similar degrees of effectiveness as in the scid mouse model. These results indicate that scid mice may be suitable for assessing therapeutic approaches to human B cell proliferation.

L7 ANSWER 53 OF 67 MEDLINE DUPLICATE 29

92325502 Document Number: 92325502. PubMed ID: 1378075. Soluble forms of CD40 inhibit biologic responses of human B cells. Fanslow W C; Anderson D M; Grabstein K H; Clark E A; Cosman D; Armitage R J. (Department of Immunology, Immunex Research and Development Corporation, Seattle, WA 98101.) JOURNAL OF IMMUNOLOGY, (1992 Jul 15) 149 (2) 655-60. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We have expressed the CD40 surface Ag as both a soluble 28-kDa molecule and a 57-kDa Fc fusion protein containing the human **IgG1** Fc region. Soluble CD40 and the Fc fusion protein inhibited the proliferative response of anti-IgM-activated human B cells to the CD40 mAb G28-5. Similarly, G28-5- and IL-4-induced IgE secretion from PBMC depleted of T cells was effectively blocked by both forms of soluble CD40. Although the soluble constructs of CD40 had only a minimal inhibitory effect on IL-4-mediated proliferation of anti-IgM-activated B cells, IL-4-induced soluble **CD23** shedding from both PBMC and T cells depleted of PBMC, and IgE secretion from PBMC, were significantly reduced in a concentration-dependent manner when soluble CD40 was present in the culture. The data presented demonstrate that both soluble forms of the CD40 molecule are biologically active, and suggest that the ligand for CD40 is inducible in IL-4-stimulated cultures and that it mediates both shedding of sCD23 and IgE secretion.

L7 ANSWER 54 OF 67 MEDLINE DUPLICATE 30

93005759 Document Number: 93005759. PubMed ID: 1382743. Establishment of a sensitive radioimmunoassay for the detection of human IgE-binding factor (soluble **CD23**). Yanagihara Y; Kiniwa M; Kajiwara K; Shida T. (Clinical Research Center for Allergy, National Sagamihara Hospital, Kanagawa, Japan.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1992) 98 (3) 189-99. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB A monoclonal **antibody** (mAb) specific to low-affinity receptor for IgE (FceRII/**CD23**) was established by the fusion of spleen cells of BALB/c mice immunized with the FceRII+ human B lymphoblastoid cell line (RPMI 8866) with mouse myeloma P3U1. Four mAbs, (10/3 **IgG1**, 11/4 **IgG1**, 10/2 IgG2b and 15/6 IgM), almost completely inhibited the IgE binding to FceRII+ cells but not to FceRII- cells. More directly, they were demonstrated to react only with 43-kD component (FceRII of the cell lysate of RPMI 8866 cells by sodium dodecyl sulfate polyacrylamide gel electrophoresis and Western blot analysis. Since they have a different epitope specificity, a solid-phase

radioimmunoassay (RIA) for the measurement of IgE-binding factor (IgE-BF) was established. It was found that the RIA with the use of 10/3 and 125I-labeled 11/4 or 12/2 gave good results in the detection of IgE-BF derived from B cells and monocytes as well as of T-cell-derived IgE-BF. More importantly, serum IgE-BF was also quantitatively measured by this RIA. Although increased serum levels of IgE-BF were observed in atopic patients, serum IgE-BF was decreased rather than increased in patients with very high serum IgE. This phenomenon may be explained by the decreased ability of the patients' B cells to spontaneously release IgE-BF in vitro.

L7 ANSWER 55 OF 67 MEDLINE DUPLICATE 31
91271264 Document Number: 91271264. PubMed ID: 1828884. Purification of murine suppressive factor of allergy into distinct **CD23** -modulating and IgE-suppressive proteins. Matsushita S; Marcelletti J F; Katz L R; Katz D H. (Division of Immunology, Medical Biology Institute, La Jolla, CA 92037.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1991 Jun 1) 88 (11) 4718-22. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The murine suppressive factor of allergy (SFA) has been purified from a T-cell hybridoma and found to consist of two functionally and biochemically distinct protein molecules. One protein (17 kDa) modulates the low-affinity Fc receptor for IgE on lymphocytes (i.e., **CD23**); it decreases the binding avidity of IgE to **CD23**-bearing B cells without affecting quantitative expression of **CD23** and is thus designated epsilon-receptor-modulating protein. The second protein (30 kDa) suppresses IgE biosynthesis (i.e., SFA). This purified SFA suppresses interleukin 4-induced IgE and **IgG1** synthesis by lipopolysaccharide-activated spleen cells but has no effect on other **antibody** isotypes; since the activity of SFA is not blocked by anti-interferon gamma monoclonal **antibody**, it is thus distinct from interferon gamma. The data presented indicate that epsilon-receptor-modulating protein and SFA are protein molecules that are involved in modulating the **CD23** molecule and IgE **antibody** synthesis, respectively.

L7 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS
1991:490415 Document No. 115:90415 Lack of Fc.epsilon.RII expression by murine B cells after in vivo immunization is directly associated with Ig secretion and not Ig isotype switching. Snapper, Clifford M.; Holley, Jeffrey J.; Urban, Joseph F., Jr.; Finkelman, Fred D. (Dep. Pathol., Uniformed Serv. Univ. Health Sci., Bethesda, MD, 20814, USA). Journal of Immunology, 146(7), 2161-8 (English) 1991. CODEN: JOIMA3. ISSN: 0022-1767.

AB The low affinity Fc receptor for IgE (Fc.epsilon.RII) has been reported to be absent from normal murine and human B cells that express a membrane (m)Ig isotype other than mIgM or mIgD in vivo. This would suggest that Fc.epsilon.RII expression is specifically lost after in vivo Ig isotype switching. The authors demonstrate that during a murine immune response to the bacterium Brucella abortus, to goat anti-mouse IgD (G.alpha.M.delta.) **antibody**, or to infection with the nematode parasites Nippostrongylus brasiliensis or Heligmosomoides polygyrus, Fc.epsilon.RII expression is low or absent on virtually all B cells secreting IgM, **IgG1**, IgG2a, and IgE. However, up to 50% of B cells that express mIgG1 after G.alpha.M.delta. injection continue to express Fc.epsilon.RII. These mIgG1+ Fc.epsilon.RII+ cells secrete little, if any, **IgG1** when placed in vitro, in contrast to their mIgG1+ Fc.epsilon.RII- counterparts. The mIgG1+ Fc.epsilon.RII+ cells may be a transitional cell population, because they undergo substantial loss of Fc.epsilon.RII in culture, unlike mIgM+ Fc.epsilon.RII+ cells, which maintain const. levels of Fc.epsilon.RII throughout a comparable culture period. Thus, low or absent expression of Fc.epsilon.RII after immunization in vivo is directly assocd. with B cell differentiation to Ig

prodn. in the presence or absence of Ig isotype switching. However, all post-switched B cells may eventually lack Fc.epsilon.RII expression, independently of their differentiative state.

L7 ANSWER 57 OF 67 SCISEARCH COPYRIGHT 2003 ISI (R) DUPLICATE 32
91:565320 The Genuine Article (R) Number: GJ565. CHARACTERIZATION OF NEW RAT ANTI-MOUSE IGE MONOCLONALS AND THEIR USE ALONG WITH CHIMERIC IGE TO FURTHER DEFINE THE SITE THAT INTERACTS WITH FC-EPSILON-RII AND FC-EPSILON-RI. KEEGAN A D; FRATAZZI C; SHOPES B; BAIRD B; CONRAD D H (Reprint). DEPT MICROBIOL & IMMUNOL, BOX 678, MCV STN, RICHMOND, VA, 23298; STANFORD UNIV, DEPT CELL BIOL, STANFORD, CA, 94305; JOHNS HOPKINS UNIV, GOOD SAMARITAN HOSP, DEPT MED, DIV MOLEC RHEUMATOL, BALTIMORE, MD, 21239; BECTON DICKERSON RES CTR, MT VIEW, CA, 94039; CORNELL UNIV, DEPT CHEM, ITHACA, NY, 14853. MOLECULAR IMMUNOLOGY (1991) Vol. 28, No. 10, pp. 1149-1154. Pub. country: USA. Language: ENGLISH.

AB *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

Three rat monoclonal **antibodies** specific for mouse IgE (C12B9, 23G3, and B1E3) were established by using monoclonal anti-DNP mouse IgE (mIgE) as immunogen. These **antibodies**, as well as a fourth, (R1E4) were characterized. It was found that one **antibody** (C12B9) recognizes an allotypic determinant (Igh-7a) found on the C-epsilon chain of mIgE. **Antibody** cross-blocking studies and epitope mapping studies using recombinant mIgE indicated that 3 **antibodies** (C12B9, R1E4 and 23G3) were directed against the C-epsilon-3 domain while one (B1E3) was directed against the C-epsilon-4 domain. A highly specific sandwich RIA for mIgE was developed using these **antibodies**. Use of these monoclonal anti-mIgE **antibodies** in conjunction with recombinant chimeric mIgE-human **IgG1** molecules, demonstrated that the C-epsilon-3 domain is important in the binding of mIgE to the murine B cell Fc-epsilon-RII as well as to the murine mast cell Fc-epsilon-RI. The presence of the C-epsilon-4 domain influenced the binding of the recombinant IgE to the Fc-epsilon-RII; in contrast to the C-epsilon-4 domain had no effect on binding to the Fc-epsilon-RI.

L7 ANSWER 58 OF 67 CAPLUS COPYRIGHT 2003 ACS
1991:581023 Document No. 115:181023 Induction of intracellular calcium mobilization and cytotoxicity by hybrid mouse monoclonal **antibodies**. Fc.gamma.RII regulation of Fc.gamma.RI-triggered functions or signaling?. Koolwijk, Pieter; Van de Winkel, Jan G. J.; Pfefferkorn, Lorraine C.; Jacobs, Cor W. M.; Otten, Isabelle; Spierenburg, Gerrit T.; Bast, Bert J. E. G. (Dep. Mol. Biol. Biotechnol., Univ. Utrecht, Utrecht, Neth.). Journal of Immunology, 147(2), 595-602 (English) 1991. CODEN: JOIMA3. ISSN: 0022-1767.

AB The interaction was studied of bispecific mouse mAb with human IgG Fc receptors, and their ability was assessed to activate the monocytic cell line U937. Binding of monomeric hybrid anti-HuIgA1/HRP (horseradish peroxidase) mAb to the high-affinity IgG receptor, Fc.gamma.RI, on U937 cells was only obsd. when mAb with one or more mIgG2a H chains (hybrid mIgG1-2a, mIgG2a-2b, and mIgG2a-2a) were used. These Fc.gamma.RI-bound hybrid mAb were capable of enhancing the internal free cytosolic Ca2+ concn. ([Ca2+]i) in U937 cells only when bound mIgG was cross-linked using F(ab')2 fragments of goat anti-mIg **antibody**. A similar increase in [Ca2+]i was obsd. when Fc.gamma.R-bound hybrid mIgG1-2a mAb were cross-linked using goat anti-mIgG1 **antibody**, showing that the hybrid mAb themselves mediate the induction of Ca2+ increase. Remarkably, anti-Fc.gamma.RII mAb IV.3 was able to inhibit the Ca2+ increase induced via mIgG2a-1 or mIgG1-2a hybrid mAb completely, despite the fact that no effect of IV.3 on binding of monomeric hybrid mIgG1-2a or mIgG2a-1 mAb to U937 was detd. The hybrid mAb also induced lysis of HuIgA1-coated E using U937 effector cells. This lysis was completely inhibited by preincubation of U937 cells with mIgG2a mAb TB-3, which blocks Fc.gamma.RI via its Fc-part Kurlander phenomenon . In contrast, Fc.gamma.RII-blocking mAb

IV.3 and CIKM5 caused a significant enhancement of the **antibody**-dependent cellular cytotoxicity (ADCC) activity mediated by hybrid mIgG1-2a and mIgG2a-2b mAb. This enhancement did not occur when the parental anti-HuIgA1/2a or the hybrid anti-HuIgA1/HRP/2a-2a mAb were evaluated for ADCC activity. These findings suggest that hybrid mAb not only can bind to Fc.gamma.RI, but can mediate functional activation of myeloid cells. Given the effect of mAb IV.3 on [Ca2+]i changes and ADCC triggered through **IgG1**-2a mAb, Fc.gamma.RII may have a role in the regulation of Fc.gamma.RI-triggered functions or signaling.

L7 ANSWER 59 OF 67 MEDLINE DUPLICATE 33
91100752 Document Number: 91100752. PubMed ID: 1824774. Suppression by IL-2 of IgE production by B cells stimulated by IL-4. Miyajima H; Hirano T; Hirose S; Karasuyama H; Okumura K; Ovary Z. (Division of Pathobiology, Juntendo University, School of Medicine, Tokyo, Japan.) JOURNAL OF IMMUNOLOGY, (1991 Jan 15) 146 (2) 457-62. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB IgE production was obtained from B cells of BALB/c or nude mice when these cells were cultured with IL-4 plus LPS. IL-2 added to these cultures at the start (day 0), 1 or 2 days later completely suppressed the production of IgE. The production of **IgG1** was also inhibited, but only if IL-2 was added on day 0. The production of other isotypes (IgM, IgG2a, IgG2b) was only slightly decreased by addition of IL-2. No suppression of IgE or **IgG1** production was observed if monoclonal anti-IL-2 was added, whereas anti-IFN-gamma had no effect on the suppression of the production of these isotypes. The expression of **CD23** on the third day of culture on B cells stimulated with LPS and IL-4 was markedly decreased when IL-2 was added to the cultures on day 0. Addition of monoclonal anti-IL-2 suppressed all effects produced by IL-2, whereas addition of anti-IFN-gamma had no effect. These results show that the suppression by IL-2, at least for the first signaling processes, are different from the suppression produced by IFN-gamma.

L7 ANSWER 60 OF 67 MEDLINE DUPLICATE 34
91339180 Document Number: 91339180. PubMed ID: 1831407. Primary anti-trinitrophenyl memory cells investigated by plaque-forming cells and ELISA. Ueda A; Leu J; Ovary Z. (Department of Pathology, New York University Medical School, New York 10016.) CELLULAR IMMUNOLOGY, (1991 Sep) 136 (2) 388-401. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

AB Primary anti-trinitrophenyl **antibody** production was investigated from spleen cells of mice immunized with trinitrophenylated-keyhole limpet hemocyanin, using the plaque-forming cell method and ELISA. Cells taken 5 days after antigen injection do not produce IgE, but do produce IgM and **IgG1** anti-trinitrophenyl **antibodies** as demonstrated by plaque-forming cells. Substantial increase of IgM, **IgG1**, and IgE **antibody** production was seen from cells taken 7 days after immunization, followed by a rapid decline. By ELISA it was seen that cells taken 3 days after immunization already produce small amounts of anti-trinitrophenyl **antibodies**. Presence of antigen from the start of the cultures did not increase **antibody** production from cells taken 3 days after immunization, but potentiated **antibody** secretions from cells taken 5 days or later after immunization. This potentiation was interpreted as recruitment of **antibody**-forming cells from early memory B cells. The presence of IL-4 from the start of the cultures had no appreciable effect. Cell sorting with specific **antibody**-coated magnetic beads showed that plaque-forming cells from nonsorted cells, membrane IgE+ or membrane IgE- cells secreted similar amounts of anti-trinitrophenyl **IgG1** and IgE **antibodies**. No difference in anti-trinitrophenyl IgM, **IgG1**, or IgE production was found in controls; cells sorted negatively or positively for **CD23**. The data show that memory B cells can be demonstrated already on day 5 after immunization, and their

antigen-induced **antibody** secretion is IL-4 dependent.

L7 ANSWER 61 OF 67 MEDLINE DUPLICATE 35
92035709 Document Number: 92035709. PubMed ID: 1834378. Cell-bound IgE and increased expression of Fc epsilon-receptors on dendritic cells in cutaneous infiltrates of mycosis fungoides. Preesman A H; Van de Winkel J G; Magnusson C G; Toonstra J; van der Putte S C; van Vloten W A. (Department of Dermatology, University Hospital Utrecht, The Netherlands.) CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1991 Nov) 86 (2) 246-51. Journal code: 0057202. ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Skin biopsies of 31 non-atopic patients, 20 with mycosis fungoides, six with psoriasis and five with contact dermatitis, and of five non-atopic healthy controls were compared for the presence of cell-bound IgE and vacant IgE binding sites. IgE+ cells were demonstrated in the cutaneous infiltrate of nine (45%) patients with mycosis fungoides, two (33%) with psoriasis and one (20%) with contact dermatitis. Following pre-incubation of skin sections with IgE myeloma protein to saturate vacant IgE-binding sites, 14 out of 16 patients (88%) with stage I mycosis fungoides, five (83%) patients with psoriasis and one (20%) with contact dermatitis showed an increase in the number of IgE+ cells. While cell-bound IgE was positively related to serum IgE levels the expression of IgE-binding sites was not. All IgE+ cells were HLA-DR+ dendritic cells identified as either macrophages (CD68+, CD14+) or Langerhans cells (CD1+). Skin biopsies of non-atopic healthy controls or clinically uninvolved skin in mycosis fungoides had neither any IgE+ cells nor any vacant binding sites. Inhibition studies with **IgG1**, IgG4 and IgE myeloma proteins as well as with several enzymatic fragments of IgE demonstrated that IgE interacted with Fc epsilon-receptors through isotype-specific structures on the Fc epsilon-fragment. Four anti-**CD23** monoclonal **antibodies**, however, were unable to stain vacant Fc epsilon-receptors nor could they block IgE-binding. We hypothesize that locally-secreted lymphokines, like IL-4 or interferon-gamma, induce Fc epsilon-receptors on dendritic cells in the cutaneous infiltrate and that these receptors become occupied in parallel with elevated serum IgE levels.

L7 ANSWER 62 OF 67 MEDLINE DUPLICATE 36
91006273 Document Number: 91006273. PubMed ID: 2145164. Induction of B cell activities by interleukin 4 is inhibited by a receptor-specific monoclonal **antibody** in vitro. Maliszewski C R; Sato T A; Vanden Bos T; Beckmann M P; Grabstein K H. (Department of Immunology, Immunex Corporation, Seattle, WA 98101.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1990 Aug) 20 (8) 1735-40. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB The effects of interleukin (IL) 4 on B cell growth and differentiation are mediated through binding of IL 4 to a specific cell surface receptor. The murine T cell IL 4 receptor (IL 4R) has recently been cloned and monoclonal **antibodies** (mAb) which bind specifically to the IL 4R have been developed. The ability of two of these anti-IL 4R mAb (M1 and M2) to inhibit IL 4-induced B cell functions in vitro was examined. The M1 mAb inhibited the ability of IL 4 to induce B cell proliferation in a dose-related fashion. The inhibition was specific for proliferation induced by IL 4 in that the **antibody** did not affect induction of proliferation by IL 1. Similarly, M1 inhibited IL 4-dependent B cell differentiation as measured by induction of **IgG1** and IgE secretion, decreased IgG3 secretion, increased Ia expression, and increased Fc epsilon R (**CD23**) expression. In contrast, the anti-IL 4R-specific mAb M2 had no effect upon any of these activities. The ability of M1 but not M2 to inhibit IL 4-induced B cell growth and differentiation correlated with the inhibition of binding of radiolabeled IL 4 by M1. These reagents should be valuable tools with which to analyze the involvement of IL 4 in immune responses.

L7 ANSWER 63 OF 67 MEDLINE DUPLICATE 37
90278152 Document Number: 90278152. PubMed ID: 2191055. Fc receptors for IgE and interleukin-4 induced IgE and IgG4 secretion. Spiegelberg H L. (Department of Immunology, Research Institute of Scripps Clinic, La Jolla, California.) JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1990 Jun) 94 (6 Suppl) 49S-52S. Ref: 42. Journal code: 0426720. ISSN: 0022-202X. Pub. country: United States. Language: English.

AB IgE binds to two types of Fc receptors, called Fc epsilon R1 (or high-affinity Fc epsilon R) and Fc epsilon R2 (or low-affinity Fc epsilon R). The Fc epsilon R1 is composed of four polypeptide chains, one alpha, one beta, and two gamma chains. The alpha chain contains the IgE binding site and is a member of the immunoglobulin supergene family. The Fc epsilon R2, also called **CD23**, consists of one polypeptide chain which shows homology to animal lectin receptors. Fc epsilon R1 are expressed on mast cells and basophils. Crosslinking of the Fc epsilon R1 induces immediate release of mediators of inflammation such as histamine and leukotrienes and delayed secretion of interleukins 4, 5, and 6. Fc epsilon R2 are expressed on resting mu delta + B cells, monocytes/macrophages (M phi), eosinophils, and platelets but rarely on T cells. Interleukin-4 upregulates Fc epsilon R2 expression on B cells and M phi. The functions of Fc epsilon R2 on the different cell types are not fully established and are controversial. Fc epsilon R2 on M phi, eosinophils, and platelets mediate cytotoxicity to schistosomules, enhance phagocytosis, and induce the release of granule enzymes. However, M phi from patients with atopic dermatitis expressing significantly more Fc epsilon R2 than M phi from normals do not release more leukotriene C4, prostaglandin E2, or beta-glucuronidase after incubation with aggregated IgE than normal monocytes. Furthermore, aggregated **IgG1** is much more efficient than IgE in inducing mediator release from M phi and **IgG1 antibodies** are not known to induce immediate-type hypersensitivity reactions. Therefore, definitive proof that Fc epsilon R2 are involved in the pathogenesis of allergic disorders is still lacking. IL-4 appears to play a central role in immediate-type hypersensitivity. It induces human B cells to secrete IgE and IgG4, Ig isotypes typical for **antibodies** to helminthic parasites and allergens. IL-4 stimulates mast cell growth and upregulates Fc epsilon R2 expression. Interferon-gamma and IL-2 inhibit the IL-4-induced IgG4 and IgE secretion. Whether the abnormally high IgE **antibody** production in atopic patients is the result of overproduction of IL-4 or deficient IFN-gamma/IL-2 production is presently unknown.

L7 ANSWER 64 OF 67 MEDLINE DUPLICATE 38
90278143 Document Number: 90278143. PubMed ID: 2191049. Fc receptors of human Langerhans cells. Schmitt D A; Bieber T; Cazenave J P; Hanau D. (Laboratoire d'Histocompatibilite, Centre Regional de Transfusion Sanguine, Strasbourg, France.) JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1990 Jun) 94 (6 Suppl) 15S-21S. Ref: 36. Journal code: 0426720. ISSN: 0022-202X. Pub. country: United States. Language: English.

AB Receptors for the Fc fragment of immunoglobulins (Fc R) exhibit specificities for a wide variety of immunoglobulin classes and subclasses. In humans, at least three distinct classes of receptors for the Fc fragments of IgG (Fc gamma RI, II, III) and two classes of receptors for the Fc fragments of IgE (Fc epsilon RI, II) have been characterized. These classes were largely defined on the basis of their affinities for different immunoglobulin subclasses and their reactivities with monoclonal anti-receptor **antibodies**. Among these FcR, in healthy individuals, epidermal Langerhans cells (LC) express only the Fc gamma RII/CDw32. This FcR--a member of the immunoglobulin superfamily--is only present on about 5% of freshly isolated OKIa positive cells, as determined by rosette assays. It has a Mr of 4[illegible] kDa, is trypsin resistant, binds polymeric human IgG and murine **IgG1**-coated erythrocytes, and reacts with anti-CDw32 monoclonal **antibodies** (MoAb). LC

internalize Fc gamma RII by receptor-mediated endocytosis. After 48 h of culture, human LC loose their Fc gamma RII, as revealed by flow cytometry. While the function(s) of the Fc gamma RII on human LC remain(s) unknown, this receptor may be primarily involved, like the Fc gamma RII present on mouse macrophages, in the clearance of extra-cellular immune complexes. In patients with atopic dermatitis having an elevated IgE serum level, beside an increased expression of the Fc gamma RII by LC located on lesional skin, IgE-bearing epidermal and dermal LC are present, again essentially on lesional skin. Double immunolabeling on cryosections reveals that on lesional skin only about 50% of the epidermal CD1a positive cells bear IgE. This capacity of LC to bind IgE molecules appears to be due to the presence of a specific Fc epsilon R. While the class of this Fc epsilon R still remains unclear, it appears to have some particularities: i) an associated expression with the CD1a antigen, ii) an affinity for IgG, and iii) a trypsin resistance. In vitro, human recombinant interleukin (IL)-4 and/or interferon (IFN)-gamma are able to induce the synthesis and expression of Fc epsilon RII/**CD23** on a percentage of normal human epidermal LC. This Fc epsilon RII seems to be functional since it binds IgE molecules, this binding being prevented by preincubation with anti-**CD23** MoAb.(ABSTRACT TRUNCATED AT 400 WORDS)

L7 ANSWER 65 OF 67 MEDLINE DUPLICATE 39

90017517 Document Number: 90017517. PubMed ID: 2529541. Low-affinity IgE receptor (**CD23**) function on mouse B cells: role in IgE-dependent antigen focusing. Kehry M R; Yamashita L C. (Department of Immunology, DNAX Research Institute of Molecular and Cellular Biology, Inc., Palo Alto, CA 94304-1104.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1989 Oct) 86 (19) 7556-60. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB B-cell surface immunoglobulin very efficiently focuses specific protein antigens for presentation to T cells. We have demonstrated a similar role in antigen focusing for the low-affinity Fc epsilon receptor (Fc epsilon RII) on mouse B lymphocytes. B cells treated with an IgE monoclonal **antibody** to 2,4,6-trinitrophenyl (TNP) (IgE-B cells) were 100-fold more effective than were untreated B cells in presenting low concentrations of TNP-antigen to T cells. Blocking the binding of IgE to Fc epsilon RII on IgE-B cells with a monoclonal **antibody** to Fc epsilon RII completely eliminated this increased effectiveness. Preformed complexes of IgE anti-TNP and TNP-antigen were more effectively presented (approximately 100-fold) than TNP-antigen in the presence of nonspecific IgE. In contrast, complexes of **IgG1** anti-TNP and TNP-antigen, capable of binding to Fc gamma receptors on B cells, were presented less effectively than TNP-antigen in the presence of nonspecific **IgG1** . Antigens focused by means of Fc epsilon RII or by means of B-cell surface immunoglobulin receptors were presented at comparably low concentrations. For several reasons, Fc epsilon RII on B lymphocytes seems to be particularly effective in efficiently focusing IgE-antigen complexes.

L7 ANSWER 66 OF 67 MEDLINE DUPLICATE 40

89249392 Document Number: 89249392. PubMed ID: 2524281. Human peripheral blood T helper cell-induced B cell activation results in B cell surface expression of the **CD23** (BLAST-2) antigen. Crow M K; Kushner B; Jover J A; Friedman S M; Mechanic S E; Stohl W. (Department of Medicine, Hospital for Special Surgery, New York, New York.) CELLULAR IMMUNOLOGY, (1989 Jun 121 1) 99-112. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

AB We have developed an in vitro system to assess the early stages of B cell activation induced by peripheral blood T helper cells. Peripheral blood mononuclear cells are cultured for 16 hr with anti-CD3 monoclonal **antibody** (mAb) , T lymphocytes are then removed by sheep red blood cell rosette depletion, and expression of the B cell surface activation antigen **CD23** (BLAST-2) is assessed by indirect

immunofluorescence. Anti-CD3 mAb, but not a control anti-CD5 mAb, stimulates the expression of **CD23** on 20-50% of peripheral blood B cells cultured with autologous T cells. T cell subset depletion studies show that the CD4+ T cell subset is responsible for anti-CD3-mediated induction of **CD23** on autologous B cells. Anti-CD3-induced, T helper cell-dependent **CD23** expression is not MHC-restricted, as allogeneic combinations of T and non-T cells, cultured in the presence of anti-CD3 **antibody**, also result in the expression of B cell **CD23**. Individuals whose monocyte Fc receptors bind murine **IgG1** mAb poorly fail to trigger T cell proliferation in response to murine **IgG1** anti-CD3 mAb and also fail to express B cell **CD23** following culture of PBMC with **IgG1** anti-CD3 mAb, while the usual expression of **CD23** is seen after culture with IgG2a anti-CD3 mAb. The mechanism of anti-CD3-induced B cell activation was addressed in experiments using a two-chamber culture system. While little IL-4 activity was detected in anti-CD3-stimulated culture supernatants, optimal induction of **CD23** was observed when T and B cells were cultured together in a single chamber. This suggests that under physiologic conditions, in which quantities of lymphokine may be limiting, close physical contact between the anti-CD3-activated Th cell and B cell may be required for **CD23** expression. The anti-CD3-induced BLAST-2 assay will facilitate the analysis of Th cell-mediated B cell activation in any individual and should permit us to separately evaluate the roles of Th cells and B cells in the impaired immunoregulation characteristic of autoimmune disorders.

L7 ANSWER 67 OF 67 MEDLINE

89053481 Document Number: 89053481. PubMed ID: 2973440. Immunoglobulin E and immunoglobulin G subclass distribution in vivo and relationship to in vitro generation of interferon-gamma and neopterin in patients with severe atopic dermatitis. Reinhold U; Pawelec G; Wehrmann W; Herold M; Wernet P; Kreysel H W. (Immunology Laboratory, Medizinische Klinik, Tubingen, FRG.) INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY, (1988) 87 (2) 120-6. Journal code: 0404561. ISSN: 0020-5915. Pub. country: Switzerland. Language: English.

AB In vitro interferon-gamma (IFN gamma) and neopterin generation by peripheral blood mononuclear cells (PBMC) from 15 patients with severe atopic dermatitis (AD) and 10 healthy controls was investigated. A significant proportion of patients had an impaired capacity to secrete IFN gamma after phytohemagglutinin (PHA) stimulation in vitro and therefore IFN gamma production was significantly lower compared to controls. Neopterin generation in vitro did not differ significantly from that of controls and no correlation between in vitro IFN gamma and neopterin production could be observed in either group. Analysis of serum IgG subclass distribution showed that patients with AD. had increased IgG4 serum concentrations while **IgG1**, IgG2 and IgG3 levels did not differ significantly from those of controls. Surface marker analysis revealed increased numbers of **CD23**+ lymphocytes in patients with AD which was positively correlated with the serum IgG4 and IgE concentration. Furthermore, a significant correlation was found between IFN gamma generation in vitro and IgE and IgG4 concentration in vivo in AD. The data suggest that a possible dysregulation of IFN gamma, interleukin-4 or other lymphokine interleukin-4 or other lymphokine production may be related to increased IgE and IgG4 production and seems to be an important factor in the pathogenesis of AD.

=> d his

FILE 'HOME' ENTERED AT 12:35:12 ON 16 JAN 2003

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 12:35:17 ON 16 JAN 2003

pI-(3;NIP/IgE), in the absence of **CD23** cross-linking, induced an immune response. As the number of natural epitopes for human **antibodies** on Der pI was less than five, we conclude that, in vivo, complexes consisting of Der pI/IgG will be directed to antigen-presenting cells expressing the high-affinity receptor for IgG (CD64), whereas IgE will allow antigen presentation by **CD23** -expressing cells, including B cells.

L9 ANSWER 3 OF 3 SCISEARCH COPYRIGHT 2003 ISI (R) DUPLICATE 2
91:565320 The Genuine Article (R) Number: GJ565. CHARACTERIZATION OF NEW RAT ANTI-MOUSE IGE MONOCLONALS AND THEIR USE ALONG WITH **CHIMERIC** IGE TO FURTHER DEFINE THE SITE THAT INTERACTS WITH FC-EPSILON-RII AND FC-EPSILON-RI. KEEGAN A D; FRATAZZI C; SHOPES B; BAIRD B; CONRAD D H (Reprint). DEPT MICROBIOL & IMMUNOL, BOX 678, MCV STN, RICHMOND, VA, 23298; STANFORD UNIV, DEPT CELL BIOL, STANFORD, CA, 94305; JOHNS HOPKINS UNIV, GOOD SAMARITAN HOSP, DEPT MED, DIV MOLEC RHEUMATOL, BALTIMORE, MD, 21239; BECTON DICKERSON RES CTR, MT VIEW, CA, 94039; CORNELL UNIV, DEPT CHEM, ITHACA, NY, 14853. MOLECULAR IMMUNOLOGY (1991) Vol. 28, No. 10, pp. 1149-1154. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Three rat monoclonal **antibodies** specific for mouse IgE (C12B9, 23G3, and B1E3) were established by using monoclonal anti-DNP mouse IgE (mIgE) as immunogen. These **antibodies**, as well as a fourth, (R1E4) were characterized. It was found that one **antibody** (C12B9) recognizes an allotypic determinant (Igh-7a) found on the C-epsilon chain of mIgE. **Antibody** cross-blocking studies and epitope mapping studies using recombinant mIgE indicated that 3 **antibodies** (C12B9, R1E4 and 23G3) were directed against the C-epsilon-3 domain while one (B1E3) was directed against the C-epsilon-4 domain. A highly specific sandwich RIA for mIgE was developed using these **antibodies**. Use of these monoclonal anti-mIgE **antibodies** in conjunction with recombinant **chimeric** mIgE-human **IgG1** molecules, demonstrated that the C-epsilon-3 domain is important in the binding of mIgE to the murine B cell Fc-epsilon-RII as well as to the murine mast cell Fc-epsilon-RI. The presence of the C-epsilon-4 domain influenced the binding of the recombinant IgE to the Fc-epsilon-RII; in contrast to the C-epsilon-4 domain had no effect on binding to the Fc-epsilon-RI.

=> s l7 and monoclonal
L10 35 L7 AND MONOCLONAL

=> s l10 and humanized
L11 1 L10 AND HUMANIZED

=> d l11 cbib abs

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**.
Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. English . CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980508.
AB The authors disclose the prepn. and characterization of murine **monoclonal** and **humanized antibodies** which bind

to the **CD23** (Fc.epsilon.RII receptor, antigen. In one example, **humanized IgG1**, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

=> dup rmeove l10
ENTER REMOVE, IDENTIFY, ONLY, OR (?):remove
'RMEOVE' IS NOT VALID. VALID FILE NAMES ARE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS'
You have entered a file name of duplicates to keep that is not referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.

=> dup remove l10
PROCESSING COMPLETED FOR L10
L12 35 DUP REMOVE L10 (0 DUPLICATES REMOVED)

=> d l12 1-35 cbib abs

L12 ANSWER 1 OF 35 SCISEARCH COPYRIGHT 2003 ISI (R)
2001:329090 The Genuine Article (R) Number: 420KX. IgE-mediated suppression of primary **antibody** responses in vivo. Karlsson M C I; De Stahl T D; Heyman B (Reprint). Uppsala Univ, Rudbeck Lab, Dept Genet & Pathol, SE-75185 Uppsala, Sweden (Reprint). SCANDINAVIAN JOURNAL OF IMMUNOLOGY (APR 2001) Vol. 53, No. 4, pp. 381-385. Publisher: BLACKWELL SCIENCE LTD. P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND. ISSN: 0300-9475. Pub. country: Sweden. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The ability of immunoglobulin (Ig)G to feedback suppress **antibody** (Ab) responses is a well known property clinically used to prevent haemolytic disease of newborns. We recently found that IgG was able to suppress the primary Ab response to sheep red blood cells (SRBC) in mice lacking the known Fc-receptors for IgG. In addition, IgE and F(ab')(2) fragments of IgG were able to suppress the response to SRBC in wild-type mice. These results suggested that the IgG-mediated suppression can take place independently of the IgG (Fc) portion and that masking of the epitopes is an important mechanism. In the present report we investigated whether the suppression caused by IgE is Fc-dependent. **Monoclonal** IgE anti-2,4,6-trinitrophenyl (TNP), administered with TNP-coupled SRBC (SRBC-TNP), can induce an efficient suppression in mice lacking Fc gamma RI f RIII + Fc epsilon RI towing to the lack of the common gamma chain, FcR gamma-, Fc gamma RIIB or Fc epsilon RII (**CD23**). Because the known IgE-binding receptors are Fc epsilon RI, **CD23**, Fc gamma RIIB and Fc gamma RIII, the results suggest that also the IgE-mediated suppression can take place independently of the Fc-receptors. A slightly less efficient suppression in **CD23** -deficient animals, suggests a minor involvement of this receptor.

L12 ANSWER 2 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2001115522 EMBASE **CD23** exhibits negative regulatory effects on allergic sensitization and airway hyperresponsiveness. Hazeku A.; Takeda K.; Hamelmann E.; Loader J.; Joetham A.; Redai I.; Irvin C.G.; Lee J.J.; Hikutani H.; Conrad D.; Gelfand E.W., Jr. E.W. Gelfand, Department of Pediatrics, Natl. Jewish Med. and Res. Center, 1400 Jackson Street, Denver, CO 80206, United States. American Journal of Respiratory and Critical Care Medicine (2001) 163 3 I 952-961 2001.
Refs: 35.
ISSN: 1073-449X. CODEN: AJCMED. Pub. Country: United States. Language: English. Summary Language: English.

AB The effects of an anti-**CD23 monoclonal antibody** (B3B4) in **CD23**-deficient and **CD23** -overexpressing mice were compared in a murine model of allergic sensitization. After sensitization and challenge with OA, mice developed increased serum levels of OA-specific IgE and **IgG1** with airway eosinophilia and AHR when compared with nonsensitized animals. Anti-**CD23** treatment was studied under two protocols: 10-d OA aerosol exposure and intraperitoneal sensitization followed by aerosol challenge. In both protocols anti-**CD23** significantly reduced IgE and **IgG1** levels, abolished eosinophilia, and normalized AHR in BALB/c and wild-type **CD23**(+/+) mice but not in **CD23**(-/-) mice. These changes were associated with increases in IFN-.gamma. and decreases in IL-4 production, suggesting that **CD23** binding may affect not only IgE production but also the Th1/Th2 imbalance during the development of allergic AHR. Absence of **CD23** in gene-deficient mice significantly enhanced OA- specific IgE and **IgG1** levels, airway eosinophilia, and AHR when compared with **CD23**(+/+) wild-type littermates after sensitization and airway challenge. Sensitized and challenged **CD23** transgenic mice also developed eosinophilic airway inflammation and methacholine hyperresponsiveness. However, the extent of AHR, BAL, and tissue eosinophilia in these animals showed a significant negative correlation with levels of **CD23** expression on splenic T and B cells, demonstrating a limiting role of **CD23** in the development of allergic AHR.

L12 ANSWER 3 OF 35 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**.
Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.
AB The authors disclose the prepn. and characterization of murine **monoclonal** and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized **IgG1**, with mutations to eliminate Clq and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

L12 ANSWER 4 OF 35 MEDLINE
1999111232 Document Number: 99111232. PubMed ID: 9893160. Upregulated surface expression of intracellularly sequestered Igepsilon receptors (FcepsilonRII/**CD23**) following activation in human peripheral blood eosinophils. Sano H; Munoz N M; Sano A; Zhu X; Herrnreiter A; Choi J; Leff A R. (Department of Medicine, Section of Pulmonary and Critical Care Medicine.) PROCEEDINGS OF THE ASSOCIATION OF AMERICAN PHYSICIANS, 1999 Jan-Feb; 111 (1) 82-91. Journal code: 9514310. ISSN: 1081-651X. Pub. country: United States. Language: English.
AB We investigated the regulation, secretion, and surface expression of the low-affinity FcepsilonRII receptor **CD23** in eosinophils isolated from human blood using multiple **monoclonal antibodies** mAbs directed at different epitopes of human **CD23**. Substantial surface expression of **CD23** was not demonstrated in the resting state. Mean fluorescence intensity MFI measured by flow cytometry was 7.1 +/- 1.9 for 9P25 mAb p = NS and 15.7

+/- 3.8 for BU38 mAb (p <. 04) versus 5.3 +/- 1.0 for **IgG1** isotype control Ab. By contrast, MFI using BU38 mAb was 154 +/- 18 for JY-B lymphocytes (p <.0001 versus eosinophils). Despite weak surface expression, eosinophil permeabilization demonstrated substantial intracellular expression of **CD23**; MFI was 33.6 +/- 5.2 for 9P25 mAb versus 4.4 +/- 0.43 for IgG control (p <.001). Western blot analysis using both positive and negative controls demonstrated immunological identity with **CD23** on JY-B lymphocytes. Activation of eosinophils caused rapid translocation of **CD23** to the surface membrane (160 +/- 33 MFI; p <. 005), which was maximal within 30 sec. Secretory **CD23** was detected within the perfusate also at 30 sec and was fully reinternalized at 10 min. This is the first demonstration of the presence of intracellular **CD23** in human eosinophils. Our data indicate that eosinophils rarely express **CD23** on their surface but are capable of transient high-level expression and secretion with rapid reuptake of intracellular stores of **CD23**.

L12 ANSWER 5 OF 35 SCISEARCH COPYRIGHT 2003 ISI (R)
1998:146156 The Genuine Article (R) Number: YW267. Presence of activated antigen-binding B cells during immunization enhances relative levels of IFN-gamma in T cell responses. Pasare C; Morafo V; Entringer M; Bansal P; George A; Bal V; Rath S (Reprint); Durdik J M. NATL INST IMMUNOL, NEW DELHI 110067, INDIA (Reprint); NATL INST IMMUNOL, NEW DELHI 110067, INDIA; UNIV ARKANSAS, DEPT BIOL SCI, FAYETTEVILLE, AR 72701. JOURNAL OF IMMUNOLOGY (15 JAN 1998) Vol. 160, No. 2, pp. 778-787. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767. Pub. country: INDIA; USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB To examine the influence of Ag presentation by B cells on immune responses, we have used mice transgenic for an Ig heavy chain from a **monoclonal** anti-azobenzenearsonate (Ars) Ab to deliver Ag to B cells during immunization, A large proportion of transgene-expressing B cells in these mice binds Ars, while transgenic serum Ig shows poor Ars binding. Transgenic B cells present Ars proteins better than their nonhaptenated counterparts. This is associated with an increase in the proliferative responses of transgenic T cells to Ars protein immunization, Although B cell numbers in the transgenic mice are lower, many B cells in them show an activated phenotype, as identified by altered surface levels of peanut agglutinin reactivity, **CD23**, CD24, CD44, CD62L, and CD86. Even against nonhaptenated immunogens, transgenic responses show significant enhancement in the relative proportions of the Th1 cytokine IFN-gamma over the Th2 cytokines IL-4 and IL-10. Haptenated immunogens further enhance the predilection of transgenic mice to produce relatively more IFN-gamma. Consistent with this, there is an increase in IgG2a/ **IgG1** ratios in serum Abs in response to haptenated immunogens in transgenic mice, Adoptive transfer of primed hapten-specific secondary B cells into nontransgenic mice also induces an increase in relative levels of IFN-gamma in response to haptenated immunogens, Thus, presentation of immunogen in vivo by activated Ag-binding B cells contributes to enhanced immunogenicity and a Th1 cytokine bias.

L12 ANSWER 6 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
1998302014 EMBASE Inhibition of sCD23 and immunoglobulin E release from human B cells by a metalloproteinase inhibitor, GI 129471. Wheeler D.G.; Parveen S.; Pollock K.; Williams P.J.. Dr. D.G. Wheeler, Department of Cell Biology, Rhone-Poulenc-Rorer Ltd, Dagenham Research Centre, Dagenham, Essex RM10 7XS, United Kingdom. Immunology 95 1 105-111 1998.
Refs: 21.
ISSN: 0019-2805. CODEN: IMMUAM. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB Soluble **CD23** (sCD23) has been proposed to play an important role in the up-regulation of immunoglobulin E (IgE) synthesis. Production of sCD23 is dependent on the proteolytic cleavage of membrane **CD23**,

but the protease(s) involved in this process remain unknown. Preliminary data, obtained by testing a panel of protease inhibitors, suggested that this enzyme may be a zinc-dependent metalloproteinase. Therefore, we investigated the effect of a standard hydroxamate-type Zn2+ metalloproteinase inhibitor (GI 129471) on both sCD23 and IgE release from human tonsiltar B cells, stimulated with interleukin-4 (IL-4) and anti-CD40. Incubation of cells for 3 days with GI 129471 inhibited the production of sCD23 with an IC50 of 602 nM .+-. 3 nm (n=3), but by 14 days the activity of the compound against sCD23 had decreased by greater than threefold (IC50 2 .+-. 0.26 .mu.M; n=3). On the other hand, GI 129471 caused a potent inhibition of IgE production, with no apparent loss of activity over the culture period (14 days: IC50 250 nM .+-. 72 nM; n=3). Time-course studies showed that, despite loss of activity against sCD23, inhibition of sCD23 production early in the culture was able to cause a potent and long-lasting inhibitory effect on IgE. Furthermore, we also showed that the activity of GI 129471 is selective for IgE, as no effect was seen on immunoglobulin G1 (**IgG1**) or IgG4 production at test concentrations as high as 10 .mu.M. These results support the hypothesis that metalloproteinases may be involved in the proteolytic cleavage of **CD23** and subsequent regulation of IgE synthesis. Inhibition of the protease(s) responsible for such cleavage may be of value in the treatment of allergic disease.

L12 ANSWER 7 OF 35 MEDLINE
1998382632 Document Number: 98382632. PubMed ID: 9716904. K21-antigen: a molecule shared by the microenvironments of the human thymus and germinal centers. Imami N; Ladyman H M; Vincents B; al-Tubuly A; Freysdottir J; Sedibane M L; Taylor-Fishwick D A; Foxwell B M; Ritter M A. (Department of Immunology, Imperial College School of Medicine, Hammersmith Hospital, London, United Kingdom.) DEVELOPMENTAL IMMUNOLOGY, (1998) 6 (1-2) 41-52. Journal code: 9200624. ISSN: 1044-6672. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The mouse **IgG1 monoclonal antibody** (mAb) K21 recognizes a 230-kD molecule (K21-Ag) on Hassall's corpuscles in the human thymus. This mAb also stains cultured thymic epithelial cells as well as other epithelial cell lines, revealing a predominant intracellular localization. Further analysis with mAb K21 on other lymphoid tissues showed that it also stains cells within the germinal centers of human tonsils, both lymphoid (B) cells and some with the appearance of follicular dendritic cells. Double immunostaining of tonsil sections shows that K21-Ag is not expressed by T cells, whereas staining with anti-CD22 and -**CD23** mAb revealed some double-positive cells. A subpopulation of the lymphoid cells express the K21-Ag much more strongly. This K21++/**CD23**++ subpopulation of cells is localized in the apical light zone of germinal centers, suggesting that K21-Ag may be an important marker for the selected centrocytes within germinal centers and may play a role in B-cell selection and/or development of B-cell memory. Flow cytometric analysis showed that K21-Ag is expressed on the surface of a very low percentage of thymocytes, tonsillar lymphocytes, and peripheral blood mononuclear cells. Analysis of purified/separated tonsillar T and B lymphocytes showed that T cells do not express the K21-Ag; in contrast, B cells express low levels of the K21-Ag, and this together with **CD23** is upregulated after mitogenic stimulation. Our data therefore raise the possibility that the K21-Ag may play a role in B-lymphocyte activation/selection.

L12 ANSWER 9 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1999:94091 Document No.: PREV199900094091. A new set of **monoclonal antibodies** against human FcgammaRII (CD32) and FcgammaRIII (CD16): Characterization and use in various assays. Vely, Frederic; Gruel, Nadege; Monsuit, Janine; Cochet, Olivier; Rouard, Helene; Tare, Sophie; Galon, Jerome; Sautes, Catherine; Fridman, Wolf-Herman; Teillaud, Jean-Luc [1]. [1] Unite INSERM 255, Lab. Biotechnol. Anticorps, Inst. Curie, 26 rue

d'Ulm, 75248 Paris Cedex 05 France. Hybridoma, (Dec., 1997) Vol. 16, No. 6, pp. 519-528. ISSN: 0272-457X. Language: English.

AB Four mouse anti-human FcgammaRII (CD32) (6C4,2B2,3D3,93.4) (**IgG1**, kappa) and one anti-human FcgammaRIII (CD16) (7.5.4) (**IgG1**, K) MAbs were raised. An in vitro switch variant, 7.5.4Sw50 (IgG2b, kappa), was also derived from the 7.5.4 MAb. 6C4, 2B2, and 3D3 MAbs bind both FcgammaRIIa and FcgammaRIIb isoforms. Two of them (6C4 and 2B2 MAbs) allow a complete blockade of the binding of immune complexes to FcgammaRII. All three MAbs immunoprecipitate the receptor and bind both its glycosylated and nonglycosylated forms. The fourth antiFcgammaRII MAb, 93.4, directed against the intracellular region of FcgammaRIIa1/2, allows its detection by Western blotting only when it is not phosphorylated. The 7.5.4 MAb binds both FcgammaRIIIa and FcgammaRIIIb, can be used in Western blotting and does not inhibit aggregated IgG binding. ELISA using IV.3 (anti-FcgammaRIIa1/2)/6C4 and 3G8 (anti-FcgammaRIIIa/b)/7.5.4Sw50 MAb pairs make it possible to detect soluble FcgammaRIIa1/2 and FcgammaRIII, with a sensitivity of 200 pg/mL and 1 ng/mL, respectively. Surface plasmon resonance analyses indicated that the KD of two of the three anti-FcgammaRH and of the anti-FcgammaRIII are in the same order of magnitude (6C4: 0.78 nM, 2B2: 0.28 nM, 7.5.4: 0.47 nM). The anti-FcgammaRII 3D3 MAb exhibits an off-rate constant higher than the 6C4 and 2B2 MAbs and a KD of 2.19 nM.

L12 ANSWER 9 OF 35 MEDLINE

97131831 Document Number: 97131831. PubMed ID: 8977305. CD40-mediated stimulation of B1 and B2 cells: implication in autoantibody production in murine lupus. Kaneko Y; Hirose S; Abe M; Yagita H; Okumura K; Shirai T. (Department of Immunology, Juntendo University School of Medicine, Tokyo, Japan.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Dec) 26 (12) 3061-5. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB B1 cells usually show preferential responses to T cell-independent antigens. To ask whether B1 cells could respond to CD40-mediated stimulation for proliferation and differentiation, and whether CD40-mediated signals are involved in the production of autoantibodies by B1 cells, we compared responses to our newly established agonistic anti-mouse CD40 **monoclonal antibody** (mAb) between B1 and B2 cells from autoimmune-prone (NZB x NZW) F1 mice. Stimulation with this mAb induced a similar level of proliferative responses of both B1 and B2 cells, as well as an increase in expression of cell surface molecules I-A, CD54, **CD23**, CD80, and CD86. While co-stimulation with interleukin (IL)-4 markedly augmented proliferative as well as **IgG1** and IgE **antibody** responses of both B and B2 cells, co-stimulation with IL-5 augmented proliferative and IgM **antibody** responses of only B1 cells. Splenic B1, but not B2 cells from young (NZB x NZW) F1 mice spontaneously produced substantial amounts of IgM including IgM anti-DNA **antibodies**, and the levels increased in case of stimulation with anti-CD40 mAb alone, or to a greater extent with the mAb plus IL-4 and IL-5. Collectively, these results indicate that splenic B1 cells from autoimmune (NZB x NZW) F1 mice have a comparable responsiveness to the CD40-mediated stimulation to that of B2 cells, which would be a potent regulatory mechanism involved in the spontaneous production of autoantibodies by B1 cells.

L12 ANSWER 10 OF 35 MEDLINE

96239301 Document Number: 96239301. PubMed ID: 8656055. Development and characterization of a novel **monoclonal antibody** mNI-11 that induces cell adhesion of the LPS-stimulated human monocyte-like cell line U937. Ikewaki N; Inoko H. Department of Microbiology, Kitasato University School of Nursing, Kitasato, Sagamihara, Japan. JOURNAL OF LEUKOCYTE BIOLOGY, 1996 May 59 5 697-719. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.

AB A **monoclonal** immunoglobulin G1 (**IgG1**) **antibody** (mAb), designated mNI-11, was produced by immunizing mice with the lipopolysaccharide (LPS)-stimulated monocyte-like cell line U937. The reactivity of mNI-11 was tested by the indirect immunofluorescence method. The antigen defined by mNI-11 was found to be expressed on U937 cells, LPS-stimulated U937 cells, normal CD14+ cells (monocytes/macrophages), and human umbilical vein endothelial cells (HUVECs). Expression of the antigen defined by mNI-11 on HUVECs slightly increased in response to exposure to tumor necrosis factor-alpha (TNF-alpha) and phorbol myristate acetate (PMA). When the reactivity of mNI-11 and mAbs binding human differentiation antigens such as CD11a, CD11b, CD11c, CD14, CD16, CD18, **CD23**, CD28, CD29, CD31, CD43, CD44, CD45RA, CD49d, CD50, CD54, CD58, CD80, CD102, CD106, HLA-class I, or HLA-class II antigen was compared, no mNI-11 reactivity resembling that of these mAbs was found. mNI-11 markedly induced homotypic cell aggregation of U937 cells when they were stimulated with LPS. The mNI-11-induced aggregation of LPS-stimulated U937 cells, referred to as LPS-U937 cells, required neither Fc receptor engagement nor cross-linking of the antigen defined by mNI-11 because aggregation was induced by both F(ab')2 fragments and monovalent F(ab') fragments of mNI-11. The mNI-11-induced aggregation was blocked by the addition of ethylenediaminetetraacetate, and also when incubated at 4 degrees C. mAbs to CD11a/CD18 (lymphocyte-function associated antigen-1; LFA-1) and CD54 (intercellular adhesion molecule-1; ICAM-1) completely blocked the LPS-U937 cell aggregation induced by mNI-11. The LPS-U937 cell aggregation induced by mNI-11 was partially but not completely blocked by the protein kinase C inhibitors sphingosine and H-7, and was completely blocked by the protein-tyrosine kinase inhibitor genistein. Interestingly, mNI-11 markedly promoted LPS-U937 cell adhesion to HUVECs. The mNI-11-induced LPS-U937 cell adhesion to HUVECs was not reduced in the presence of LFA-1 (CD11a/CD18) or ICAM-1 (CD54) mAbs. On the other hand, LPS-U937 cells, whether treated with mNI-11 or not, sufficiently adhered to the extracellular matrix protein fibronectin, but not to laminin or collagen type I. However, mNI-11 did not markedly promote LPS-U937 cell adhesion to fibronectin. Adhesion of LPS-U937 cells treated with mNI-11 to fibronectin was completely blocked by CD29 (beta chain of very late antigens) mAb. The surface antigen recognized by mNI-11 had a molecular size of approximately 97 kDa under non-reducing conditions and approximately 117 kDa under reducing conditions, as determined by immunoblotting analysis. We found that mNI-11 recognizes an adhesion-associated molecule distinct from any previously reported in terms of its pattern of cellular distribution and molecular weight, and also found that mNI-11 has activity which induces cell adhesion/aggregation of U937 cells when stimulated with LPS.

L12 ANSWER 11 OF 35 SCISEARCH COPYRIGHT 2003 ISI (R)
96:685011 The Genuine Article (R) Number: VG477. AUTOANTIBODY-MEDIATED CAPTURE AND PRESENTATION OF AUTOANTIGEN TO T-CELLS VIA THE FC-EPSILON RECEPTOR BY A RECOMBINANT HUMAN AUTOANTIBODY FAB CONVERTED TO IGE. GUO J; QUARATINO S; JAUME J C; COSTANTE G; LONDEI M; MCLACHLAN S M; RAPOPORT B (Reprint). VET ADM MED CTR, THYROID MOL BIOL UNIT 111T, 4150 CLEMENT ST, SAN FRANCISCO, CA, 94121 (Reprint); VET ADM MED CTR, THYROID MOL BIOL UNIT 111T, SAN FRANCISCO, CA, 94121; UNIV CALIF SAN FRANCISCO, SAN FRANCISCO, CA, 94121; MATHILDA & TERENCE KENNEDY INST RHEUMATOL, SUNLEY DIV, LONDON W6 8LW, ENGLAND. JOURNAL OF IMMUNOLOGICAL METHODS (29 SEP 1996) Vol. 195, No. 1-2, pp. 91-92. ISSN: 0022-1759. Pub. country: USA; ENGLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Fc epsilon receptor **CD23** -mediated capture of IgE-antigen complexes by B cells provides a powerful antigen presenting system. Our goal was to develop a system using high affinity, human, organ-specific **monoclonal** autoantibodies for antigen capture by B cells. For this purpose, we converted a recombinant human autoantibody to TPO from a Fab (SP1.4) to an IgE molecule. Sera from all patients with autoimmune thyroid

disease contain autoantibodies with the same epitope as SP1.4. The SP1.4 H and L chain V region genes were spliced by overlap PCR to a mammalian, non-immunoglobulin signal peptide and transferred to expression vectors for human **IgG1** and kappa, respectively. After inserting the IgE constant region genes into the H chain vector, the kappa and IgE H chain vectors were expressed in SP2/0 cells. SP1.4-IgE retains its high affinity (K-d) for TPO (similar to 2 x 10(-10) M), recognizes the same epitope as Fab SP1.4 and, importantly, binds to a different epitope than does Fab TR1.9. Binding of preformed complexes of SP1.4-IgE and biotinylated TPO to EB virus transformed B cells (EBVL) was weakly detectable by flow cytometry and was displaced by unlabeled TPO. SP1.4-IgE/I-125-TPO complex binding to EBVL was much more clearly evident, was also inhibited by the addition of unlabeled TPO, and was greatly reduced by preincubation of the EBVL with anti-**CD23**. Further, autologous EBVL preincubated with SP1.4-IgE/TPO complexes stimulated proliferation of TPO-specific T cells. IgE autoantibody-mediated antigen focusing to B cells is unlikely to operate in vivo but is, instead, a powerful investigative tool.

In conclusion, SP1.4-IgE is the first **monoclonal** human autoantibody to be developed for IgE-mediated antigen presentation to T cells by EBVL. Recombinant human autoantibodies converted to IgE, possibly in combinations if their epitopes permit simultaneous binding to the same molecule, provide a unique system to generate human T cell lines and clones specific for peptides naturally processed from internalized high affinity autoantibody/autoantigen complexes.

L12 ANSWER 12 OF 35 MEDLINE

95293053 Document Number: 95293053. PubMed ID: 7774652. No role of interleukin-4 in **CD23**/IgE-mediated enhancement of the murine **antibody** response in vivo. Hjulstrom S; Landin A; Jansson L; Holmdahl R; Heyman B. (Department of Pathology, Uppsala University Hospital, Sweden.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1995 May) 25 (5) 1469-72. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Antigen-specific IgE up-regulates the specific IgM, **IgG1**, IgG2a and IgE response in vivo when given to mice together with antigen. The enhancement is mediated by the low-affinity receptor for IgE, Fc epsilon RII or **CD23**, as demonstrated both in **CD23**-deficient mice and by blocking **CD23** with anti-**CD23** **monoclonal antibodies**. A possible mechanism behind the regulatory effects of **CD23** is that the IgE/**CD23** /antigen complex is endocytosed by B cells, leading to increased antigen processing and presentation on major histocompatibility complex (MHC) class II molecules to T helper cells. In the present study we have found that the expression of **CD23** is reduced fivefold on splenic B cells in mice genetically deficient for IL-4. When IL-4-deficient mice and normal littermates were immunized with 2,4,6-trinitrophenyl (TNP)-specific IgE followed by bovine serum albumin (BSA)-TNP or with BSA-TNP alone, the BSA-specific **IgG1** and IgG2a responses were equally well augmented by IgE in all mice. In addition, a low but significant IgE response was seen even in the IL-4-deficient mice. Thus, enhancement of the **antibody** response through IgE and **CD23** occur in the absence of IL-4 and is not dependent on **CD23** up-regulation.

L12 ANSWER 13 OF 35 MEDLINE

94239956 Document Number: 94239956. PubMed ID: 8176203. **CD23** /IgE-mediated regulation of the specific **antibody** response in vivo. Gustavsson S; Hjulstrom S; Liu T; Heyman B. Department of Pathology, Uppsala University Hospital, Sweden. JOURNAL OF IMMUNOLOGY, 1994 May 15 152 10 4793-800. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We have recently reported that IgE Abs specific for TNP are able to enhance the specific IgG response in mice via the low affinity receptor for IgE, Fc epsilon RII, or **CD23**. In this study we show that IgE

can up-regulate IgM, **IgG1**, IgG2a, and the IgE response, thereby indicating the possibility of a viscious circle in the maintenance of an allergic response. One of the suggested modes of action of IgE/ **CD23** is to increase the ability of B cells to present Ag to T cells. The involvement of T cells in IgE-mediated enhancement of the Ab response was studied in several ways: nude mice were resistant to the effect of IgE and a dramatic effect on the induction of immunologic memory was seen, both by in situ secondary immunizations and in adoptive transfer systems. Basic conditions for the ability of IgE to induce enhancement were established, demonstrating critical importance of factors such as type of Ag and temporal relationship between administration of IgE and Ag. Finally, no evidence for the requirement for **CD23** for a normal (non-IgE induced) Ab response was found, although modulation of the receptor completely abrogated the IgE-induced Ab response.

L12 ANSWER 14 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
94072760 EMBASE Document No.: 1994072760. Identification of a T cell membrane protein possibly involved in IL-4- induced B cell immunoglobulin class switching to IgE. Matsushita S.; Katz D.H.. Division of Immunology, Medical Biology Institute, 11077 North Torrey Pines Road,San Diego, CA 92037, United States. Cellular Immunology 153/2 (378-391) 1994. ISSN: 0008-8749. CODEN: CLIMB8. Pub. Country: United States. Language: English. Summary Language: English.

AB The murine T cell hybridoma line, MBI-1.15, secretes a 17-kDa protein which decreases binding activity of the **CD23** molecule for its natural ligand, IgE. This protein, denoted .epsilon. receptor-modulating protein (.epsilon.RMP), was previously characterized and shown to be a novel serine protease. The present studies show that, in addition to modulating **CD23**, .epsilon.RMP costimulates with Il-4 the de novo synthesis and secretion of IgE and **IgG1** by cultured B cells. Since such costimulating activity is reminiscent of a similar synergism with IL-4 previously observed with cell membranes from activated T cells, we examined isolated membranes from the .epsilon.RMP-producing MBI-1.15 T cell line for comparable activity; indeed, as shown herein. MBI-1.15 cell membranes do exhibit this synergism. Furthermore, we show that a **monoclonal antibody** (mAb), 2E5B, specific for the 17-kDa soluble form of .epsilon.RMP, blocks the costimulating activities of both the soluble .epsilon.RMP and MBI-1.15 T cell membranes for IL-4-induced de novo synthesis of IgE by cultured B cells. This anti-.epsilon.RMP mAb also detects a 36-kDa membrane-bound protein species which appears to be related to soluble .epsilon.RMP by immunochemical criteria. The membrane-bound proteins, present on MBI-1.15 T cells, induce germ-line IgE heavy chain transcripts (I.epsilon.) in I-29 B cells independently of IL-4, and this inductive event is also specifically blocked by the 2E5B anti-.epsilon.RMP mAb. These findings suggest that T cell membrane-bound .epsilon.RMP molecules are crucial proteins involved in contact-dependent B cell class switching in the course of IgE biosynthesis. Finally, both IL-4 and .epsilon.RMP induce I.epsilon. on I-29 B cells, but neither molecule by itself can induce class switching to IgE synthesis by splenic B cells. This clearly suggests that both .epsilon.RMP and IL-4 have another important molecular effect (which may or may not be identical) on B cells, that is essential for class switching, but only when both molecules are present simultaneously is the complete mechanism of class switching manifested.

L12 ANSWER 15 OF 35 CAPLUS COPYRIGHT 2003 ACS
1993:493523 Document No. 119:93523 Murine and human cytokine CD40-L which binds to CD40, and soluble CD40 and CD40 fusion molecules. Armitage, Richard J.; Fanslow, William C.; Spriggs, Melanie K. (Immunex Corp., USA . PCT Int. Appl. WO 9309207 A1 19930429, 79 pp. DESIGNATED STATES: W: AU, CA, FI, JP, NO; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE. English . CODEN: PIXXIO. APPLICATION: WO 1992-US8991 19921023. PRIORITY: US 1991-783707 19911028; US 1991-805723 19911205.

AB The title CD40-L mols. are disclosed, as are related DNA sequences, vectors, and transformed host cells. The murine and human CD40-L polypeptides bind to the extracellular binding region of a CD40 receptor. Also provided are a CD40/**IgG1** Fc region fusion protein and a sol. CD40 protein (sCD40) comprising the extracellular portion of CD40; both the CD40/Fc and sCD40 can inhibit CD40-L or anti-CD40 **monoclonal antibody**-induced B-cell stimulation, interleukin-4-induced IgE stimulation, and interleukin-4-induced **CD23** induction in B-cells. Construction is described of a CD40/Fc DNA for prodn. of a fusion protein for use in detecting cDNA clones encoding a CD40 ligand. Also described are selection of a cell line putatively expressing CD40-L, prepn. of a cDNA library for expression cloning of murine CD40-L, cross-species hybridization methodol. used to isolate a human CD40-L homolog, anti-allergy therapeutic effects of sCD40 and CD40/Fc fusion protein, etc. Interaction of CD40 with its ligand was evidently the principal mol. interaction responsible for T-cell contact-dependent induction of B-cell growth and differentiation to both antigen-specific **antibody** prodn. and polyclonal Ig secretion.

L12 ANSWER 16 OF 35 CAPLUS COPYRIGHT 2003 ACS
1993:232271 Document No. 118:232271 T-cell proteins for B-cell Ig class switching and IgE binding modulation. Katz, David H.; Matsushita, Sho (Medical Biology Institute, USA). PCT Int. Appl. WO 9302696 A1 19930218, 75 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US6553 19920806. PRIORITY: US 1991-741671 19910807.

AB A crude protein prepn. known as suppressive factor of allergy (SFA) consists of 2 functionally and biochem. distinct proteins: (1) a 30-kDa protein which suppresses IgE biosynthesis and is distinct from .gamma.-interferon, and (2) a sol. .epsilon. receptor-modulating protein (.epsilon.RMP) of mol. wt. 17 kDa which modulates **CD23**, induces germline IgE heavy chain transcripts, and enhances IgE biosynthesis by B-cells in the presence of interleukin 4. .epsilon.RMP is a serine proteinase, decreases the avidity of binding of IgE to the **CD23** low-affinity IgE Fc receptor on B-cells without decreasing the quant. expression of **CD23**, requires CD4+ T-cells to mediate its effect on B-cells, and has a unique partial internal sequence Ala-Lys-Pro-Ala-Pro-Lys-Lys-Glu-Glu-Lys-Lys-Lys-Lys-Ala-Ala-Ala-Lys-Lys. .epsilon.RMP also exists in a 36-kDa T-cell membrane form. Both forms are useful in diagnostic assays and for therapeutically altering the immune response in mammals. A murine T-cell hybridoma which produces high titers of .epsilon.RMP is described.

L12 ANSWER 17 OF 35 SCISEARCH COPYRIGHT 2003 ISI (R)
94:3142 The Genuine Article (R) Number: MM689. SWITCHING CAPACITY OF FC-EPSILON-RII-POSITIVE AND FC-EPSILON-RII-NEGATIVE MURINE B-CELLS. FOY T M; WALDSCHMIDT T J (Reprint). UNIV IOWA, COLL MED, DEPT PATHOL, IOWA CITY, IA, 52242 (Reprint); UNIV IOWA, COLL MED, DEPT PATHOL, IOWA CITY, IA, 52242. EUROPEAN JOURNAL OF IMMUNOLOGY (DEC 1993) Vol. 23, No. 12, pp. 3208-3216. ISSN: 0014-2980. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In previous studies, our laboratory demonstrated the utility of the low affinity IgE Fc receptor (FcepsilonRII) in delineating a number of murine B cell subsets. In the spleen, the FcepsilonRII is expressed on mature conventional B cells but is absent on marginal zone B cells. In the peritoneal cavity, the receptor is present on all conventional B cells, but is not expressed on fresh peritoneal Ly1/sister B cells. The studies in this report compared the ability of these B cell populations to isotype switch. Using a lipopolysaccharide (LPS) - and interleukin (IL)-4-driven system, sort-purified FcepsilonRII- positive and -negative B cells from peritoneum and spleen were tested for switching to **IgG1**, IgE, and IgA. The results demonstrated that regardless of their source, FcepsilonRII+ B cells produced significant levels of **IgG1** and

IgE. Similar results were obtained with FcepsilonRII- (marginal zone) B cells obtained from spleen. In contrast, FcepsilonRII- (Ly1/sister) peritoneal B cells were found to produce **IgG1** and IgA, but were incapable, of secreting significant levels of IgE. Further studies tested for LPS and IL-4-induced expression of FcepsilonRII and Thy1 on the various B cell populations. These experiments demonstrated the induction of the FcepsilonRII on all B cells, regardless of their initial resting levels. Additionally, Thy1 was found to be induced only on those B cell subsets capable of producing IgE. Taken together, the results demonstrate a correlation between IgE secretion and Thy1 expression, and no apparent correlation between the presence of the FcepsilonRII and isotype commitment.

L12 ANSWER 18 OF 35 SCISEARCH COPYRIGHT 2003 ISI (R)
93:324702 The Genuine Article (R) Number: LC381. ENGAGEMENT OF CD40 LOWERS THE THRESHOLD FOR ACTIVATION OF RESTING B-CELLS VIA ANTIGEN RECEPTOR. WHEELER K (Reprint); POUND J D; GORDON J; JEFFERIS R. UNIV BIRMINGHAM SCH MED, DEPT IMMUNOL, BIRMINGHAM B15 2TT, ENGLAND (Reprint). EUROPEAN JOURNAL OF IMMUNOLOGY (MAY 1993) Vol. 23, No. 5, pp. 1165-1168. ISSN: 0014-2980. Pub. country: ENGLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Cross-linking of surface Ig (sIg) on resting B cells can generate intracellular signals; however, for T-dependent antigens to promote growth and differentiation additional surface receptors must be engaged. Ligation of CD40 can stimulate B cell proliferation in the presence of interleukin-4. A recently identified counterstructure for CD40 is found on T helper cells and is believed to represent the cognate ligand for B cell activation. This study investigates the role of CD40 as an accessory molecule in sIg-dependent B cell activation. Simultaneous ligation of sIg and CD40 by **monoclonal antibodies** (mAb) in the presence of mouse L cells which express human Fcgamma receptor type II (FcgammaRII-L cells) results in potent stimulation of small resting B cells. When CD40 is co-ligated, picomolar concentrations of mouse **IgG1** anti-mu, and anti-delta mAb can stimulate B cell proliferation. This requires interaction of the anti-Ig mAb with the FcgammaRII-L cells: a mouse IgG2a anti-mu mAb which is not recognized by FcgammaRII, was greater-than-or-equal-to 1000-fold less effective. These findings suggest a mechanism for B cell activation whereby engagement of T cells via CD40 and its cognate ligand provides potent enhancement of signals delivered through sIg. Based on these observations, models for the activation of B cells by T-dependent antigens are presented.

L12 ANSWER 19 OF 35 MEDLINE
94011854 Document Number: 94011854. PubMed ID: 8407286. Effect of immunological stimulation on the production of platelet-activating factor by rat peritoneal cells: its relevance to anaphylactic reactions. Pellon M I; Fernandez-Gallardo S; Gijon M A; Garcia M C; Liu F T; Sanchez Crespo M. (Departamento de Bioquimica y Fisiologia-CSIC, Facultad de Medicina, Valladolid, Spain.) IMMUNOPHARMACOLOGY, (1993 Jul-Aug) 26 (1) 73-82. Journal code: 7902474. ISSN: 0162-3109. Pub. country: Netherlands. Language: English.
AB The production of platelet-activating factor (PAF) by rat peritoneal cells was studied using as stimuli either **monoclonal** IgE, **IgG1** or IgG2b anti-DNP (2,4-dinitrophenyl), and DNP-BSA. Peritoneal cells sensitized in vitro with any of these **antibodies** at concentrations higher than 1 nM and challenged with 1 microM DNP-BSA produced PAF. PAF production was also elicited by preformed IgE, and IgG2b/DNP-BSA immune complexes, preferentially at a large antigen/**antibody** ratio. The production of PAF was unrelated to the activation of mast cells, since it occurred in populations depleted of mast cells by adherence to plastic dishes. Moreover, the release of [3H]serotonin from IgE-sensitized mast cells showed a time-course more rapid than PAF production and occurred in cells sensitized with IgE at

concentrations lower than those required for PAF formation. In contrast, peritoneal cells sensitized with **IgG1** and IgG2b failed to release [3H]serotonin. Rat peritoneal cells showed a significant ability to catabolize PAF by intracellular PAF-acetylhydrolase in view of both the amounts of enzyme activity assayed in cellular homogenates, and the 15-fold increase on controls of PAF quantities detected in peritoneal cells treated with phenylmethylsulfonyl fluoride (PMSF), a known inhibitor of PAF-acetylhydrolase. The PAF activity produced upon PMSF addition showed a retention time on reverse-phase HPLC which suggests structural identity to PAF produced by either immunological challenge or ionophore A23187. These data suggest that PAF formed during rat passive anaphylaxis reactions depends on the activation of mononuclear phagocytes. This production may be triggered by two types of low affinity receptors: Fc epsilon RII/**CD23** and Fc gamma R. The ability of peritoneal cells to catabolize PAF by intracellular acetylhydrolase seems unaffected by immunological stimulation.

L12 ANSWER 20 OF 35 MEDLINE
93172603 Document Number: 93172603. PubMed ID: 8382322. Suppression of IgE production by IPD-1151T (suplatast tosilate), a new dimethylsulfonium agent: (1). Regulation of murine IgE response. Yanagihara Y; Kiniwa M; Ikizawa K; Yamaya H; Shida T; Matsuura N; Koda A. (Clinical Research Center for Allergy, National Sagamihara Hospital, Kanagawa, Japan.) JAPANESE JOURNAL OF PHARMACOLOGY, (1993 Jan) 61 (1) 23-30. Journal code: 2983305R. ISSN: 0021-5198. Pub. country: Japan. Language: English.
AB The effect of IPD-1151T, a new dimethylsulfonium compound, on the IgE response was investigated in the mouse system. The oral administration of IPD-1151T to immunized BALB/c mice suppressed the primary IgE **antibody** response and depressed the elevation of serum IgE levels, whereas the same treatment did not affect the IgG **antibody** response. The enhanced expression of low-affinity IgE receptor (Fc epsilon RII/**CD23**) on the spleen cells of immunized mice was also inhibited by IPD-1151T administration. It was further demonstrated from the adoptive transfer experiment that IPD-1151T, administered to hapten-primed B cell donors, but not to carrier-primed T cell donors, exerted its suppressive influence on the hapten-specific secondary IgE **antibody** response in irradiated syngeneic recipients. Interestingly, IPD-1151T concentration-dependently inhibited the production of interleukin 4 (IL-4) by D10G4.1, known to be a typical Th2 clone. However, IPD-1151T did not suppress the production of IgE and **IgG1** by normal splenic B cells stimulated with lipopolysaccharide and IL-4. Moreover, IL-4-induced expression of Fc epsilon RII on normal spleen cells was not inhibited by the agent. These results strongly suggest that the IgE-suppressive activity of IPD-1151T is most likely due to the inhibition of IL-4 production at the T cell level.

L12 ANSWER 21 OF 35 MEDLINE
93318718 Document Number: 93318718. PubMed ID: 7687088. A study of the interrelationship between circulating IgG subclass anti-IgE autoantibodies, IgE and soluble **CD23** in asthma. Shakib F; Boulstridge L; Smith S J. (Department of Immunology, University Hospital, Queen's Medical Centre, Nottingham, U.K.) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1993 Jan-Feb) 21 1 29-4. Journal code: 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.
AB In this paper we hypothesise that circulating autoanti-IgE **antibodies**, which are found in allergic asthma patients, could potentially enhance IgE synthesis by blocking its binding to **CD23** on B lymphocytes, thereby potentiating the release of soluble fragments of **CD23** which have B cell growth-promoting activity. We have investigated this possibility indirectly by measuring soluble s **CD23** and IgG subclass anti-IgE **antibody** levels in asthmatic patients' sera, to find out if the two parameters are related. However, we were unable to show any significant correlations between serum

IgG subclass anti-IgE activities and sCD23 levels. This may have been due, at least in part, to the heterogeneous epitope specificity of the autoanti-IgE being detected. Interestingly, there was a significant inverse correlation ($p = 0.0178$) between serum IgE and sCD23 levels in asthma; an observation which underlines the notion that binding of IgE to membrane **CD23** abrogates the release of sCD23. The present study confirms and extends previous reports of significantly raised circulating levels of IgG anti-IgE in asthma patients ($p = 0.0004$), by further demonstrating that IgG anti-IgE is mostly restricted to **IgG1**. Given that **IgG1** binds very efficiently to C1q and Fc gamma Rs, our observation lends further support to the notion that IgG anti-IgE may facilitate the removal of IgE-allergen complexes by triggering IgG effector function pathways.

L12 ANSWER 22 OF 35 MEDLINE

92347407 Document Number: 92347407. PubMed ID: 1386315. Co-crosslinking Fc epsilon RII/**CD23** and B cell surface immunoglobulin modulates B cell activation. Campbell K A; Lees A; Finkelman F D; Conrad D H. (Department of Microbiology and Immunology, Virginia Commonwealth University, Richmond.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1992 Aug) 22 (8) 2107-12. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Previous studies have shown that a highly multivalent from of anti-IgD or anti-IgM, prepared by conjugating the respective **antibodies** to dextran, causes extensive B cell proliferation with ng/ml concentrations of the anti-immunoglobulin (Ig). A modification of this system has been exploited to investigate the effect of co-crosslinking the Fc epsilon RII and surface Ig by binding DNP to the dextran backbone (DNP-dextran) and employing a DNP-specific **monoclonal** IgE of either rat or mouse origin. Addition of anti-IgD-(H delta a/1)[DNP-dextran] or anti-IgM-[DNP-dextran] to purified, resting murine B cells resulted in B cell proliferation over a broad dose (0.03-30 micrograms/ml). Addition of DNP-specific rat or mouse IgE dramatically modulated the proliferative response. Proliferation in response to doses greater than 0.3 microgram/ml H delta a/1-[DNP-dextran] was consistently reduced in a dose-dependent manner in the presence of increasing amounts of IgE while proliferation to lower concentrations of H delta a/1-[DNP-dextran] was slightly enhanced or not influenced at all by the IgE anti-DNP. Interleukin-4 (IL-4) significantly increased the IgE effect, in line with its known enhancing effects on Fc epsilon RII levels. Experiments measuring Ig production rather than proliferation demonstrated that in the presence of IgE anti-DNP, B cells produced lower amounts of immunoglobulin (**IgG1** or IgM) in response to an anti-Ig signal. Control experiments demonstrated that the IgE effect on proliferation was blocked by **monoclonal** anti-Fc epsilon RII, but not anti-Fc gamma RII, thus demonstrating the necessity for IgE/Fc epsilon RII interaction. In addition, the necessity for co-crosslinking was shown by the inability of IgE anti-DNP to affect the proliferative response to H delta a/1-dextran even in the presence of various doses of DNP-dextran. These results demonstrate that co-crosslinking of sIg and the Fc epsilon RII results in an altered B cell response to anti-Ig mediated activation. IL-4 does not ablate this inhibition, in contrast to the effect of co-crosslinking Fc gamma RII and surface Ig, suggesting a model whereby IgE can modulate its own production.

L12 ANSWER 23 OF 35 MEDLINE

92395174 Document Number: 92395174. PubMed ID: 1326002. Control of human B cell tumor growth in severe combined immunodeficiency mice by **monoclonal** anti-B cell **antibodies**. Durandy A; Brousse N; Rosenberg F; De Saint Basile G; Fischer A M; Fischer A. Institut National de la Sante et de la Recherche Medicale, U 132, Hopital des Enfants-Malades, Paris, France. JOURNAL OF CLINICAL INVESTIGATION, 1992 Sep. 90 3 945-52. Journal code: 7802877. ISSN: 0021-9738. Pub. country:

United States. Language: English.

AB Severe combined immunodeficiency (scid) mice develop EBV (+)B cell tumors after infusion of EBV(+)B cells or of B cells and EBV. In this study, scid mice were infused with B cell lines derived from three patients who developed a B lymphocyte proliferative disorder after bone marrow or organ transplantation. Intraperitoneal injection of 5 x 10(6) B cells induced tumor growth in all mice, leading to death within 60 d. Human B cells were identified in spleen and bone marrow by means of immunofluorescence or EBV genome amplification, and human IgM was detected in serum. Infusion of murine **monoclonal antibodies** specific for human B cell membrane antigens CD21, CD24, and **CD23** was effective in 80% of animals, against two of the three cell lines preventing tumor development or inducing remission according to the time of treatment. The effect was **antibody** dose dependent and was optimal with four intravenous infusions of at least 0.1 mg 4 d apart. Human IgM in serum and human B cells in spleen and bone marrow became undetectable when peritoneal tumors regressed completely. Infusions of **IgG1** isotype-matched anti-CD4 **antibody** or anti-CD3 **antibody** had no effect. Tumors developed or recurred in 50% of these animals injected with one of the B cell line 3 mo after treatment was stopped. The same anti-CD21 and anti-CD24 **antibodies** had been used to treat the three patients, and shown similar degrees of effectiveness as in the scid mouse model. These results indicate that scid mice may be suitable for assessing therapeutic approaches to human B cell proliferation.

L12 ANSWER 24 OF 35 MEDLINE

92325502 Document Number: 92325502. PubMed ID: 1378075. Soluble forms of CD40 inhibit biologic responses of human B cells. Fanslow W C; Anderson D M; Grabstein K H; Clark E A; Cosman D; Armitage R J. (Department of Immunology, Immunex Research and Development Corporation, Seattle, WA 98101.) JOURNAL OF IMMUNOLOGY, (1992 Jul 15) 149 (2) 655-60. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We have expressed the CD40 surface Ag as both a soluble 28-kDa molecule and a 57-kDa Fc fusion protein containing the human **IgG1** Fc region. Soluble CD40 and the Fc fusion protein inhibited the proliferative response of anti-IgM-activated human B cells to the CD40 mAb G28-5. Similarly, G28-5- and IL-4-induced IgE secretion from PBMC depleted of T cells was effectively blocked by both forms of soluble CD40. Although the soluble constructs of CD40 had only a minimal inhibitory effect on IL-4-mediated proliferation of anti-IgM-activated B cells, IL-4-induced soluble **CD23** shedding from both PBMC and T cells depleted of PBMC, and IgE secretion from PBMC, were significantly reduced in a concentration-dependent manner when soluble CD40 was present in the culture. The data presented demonstrate that both soluble forms of the CD40 molecule are biologically active, and suggest that the ligand for CD40 is inducible in IL-4-stimulated cultures and that it mediates both shedding of sCD23 and IgE secretion.

L12 ANSWER 25 OF 35 MEDLINE

93005759 Document Number: 93005759. PubMed ID: 1382743. Establishment of a sensitive radioimmunoassay for the detection of human IgE-binding factor (soluble **CD23**). Yanagihara Y; Kiniwa M; Kajiwara K; Shida T. (Clinical Research Center for Allergy, National Sagamihara Hospital, Kanagawa, Japan.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1992) 99 (3) 299-99. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB A **monoclonal antibody** (mAb) specific to low-affinity receptor for IgE (FceRII/**CD23**) was established by the fusion of spleen cells of BALB/c mice immunized with the FceRII+ human B lymphoblastoid cell line (RPMI 8866) with mouse myeloma P3U1. Four mAbs, (11/3 **IgG1**, 11/4 **IgG1**, 10/2 IgG2b and 15/6 IgM), almost completely inhibited the IgE binding to FceRII+ cells but not to

FceRII- cells. More directly, they were demonstrated to react only with 43-kD component/FceRII of the cell lysate of RPMI 8866 cells by sodium dodecyl sulfate polyacrylamide gel electrophoresis and Western blot analysis. Since they have a different epitope specificity, a solid-phase radioimmunoassay (RIA) for the measurement of IgE-binding factor (IgE-BF) was established. It was found that the RIA with the use of 10/3 and 125I-labeled 11/4 or 12/2 gave good results in the detection of IgE-BF derived from B cells and monocytes as well as of T-cell-derived IgE-BF. More importantly, serum IgE-BF was also quantitatively measured by this RIA. Although increased serum levels of IgE-BF were observed in atopic patients, serum IgE-BF was decreased rather than increased in patients with very high serum IgE. This phenomenon may be explained by the decreased ability of the patients' B cells to spontaneously release IgE-BF in vitro.

L12 ANSWER 26 OF 35 MEDLINE

91271264 Document Number: 91271264. PubMed ID: 1828884. Purification of murine suppressive factor of allergy into distinct **CD23** -modulating and IgE-suppressive proteins. Matsushita S; Marcelletti J F; Katz L R; Katz D H. (Division of Immunology, Medical Biology Institute, La Jolla, CA 92037.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1991 Jun 1) 88 (11) 4718-22. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The murine suppressive factor of allergy (SFA) has been purified from a T-cell hybridoma and found to consist of two functionally and biochemically distinct protein molecules. One protein (17 kDa) modulates the low-affinity Fc receptor for IgE on lymphocytes (i.e., **CD23**); it decreases the binding avidity of IgE to **CD23**-bearing B cells without affecting quantitative expression of **CD23** and is thus designated epsilon-receptor-modulating protein. The second protein (30 kDa) suppresses IgE biosynthesis (i.e., SFA). This purified SFA suppresses interleukin 4-induced IgE and **IgG1** synthesis by lipopolysaccharide-activated spleen cells but has no effect on other **antibody** isotypes; since the activity of SFA is not blocked by anti-interferon gamma **monoclonal antibody**, it is thus distinct from interferon gamma. The data presented indicate that epsilon-receptor-modulating protein and SFA are protein molecules that are involved in modulating the **CD23** molecule and IgE **antibody** synthesis, respectively.

L12 ANSWER 27 OF 35 SCISEARCH COPYRIGHT 2003 ISI (R)

91:565320 The Genuine Article (R) Number: GJ565. CHARACTERIZATION OF NEW RAT ANTI-MOUSE IGE **MONOCLONALS** AND THEIR USE ALONG WITH CHIMERIC IGE TO FURTHER DEFINE THE SITE THAT INTERACTS WITH FC-EPSILON-RII AND FC-EPSILON-RI. KEEGAN A D; FRATAZZI C; SHOPES B; BAIRD B; CONRAD D H (Reprint). DEPT MICROBIOL & IMMUNOL, BOX 678, MCV STN, RICHMOND, VA, 23298; STANFORD UNIV, DEPT CELL BIOL, STANFORD, CA, 94305; JOHNS HOPKINS UNIV, GOOD SAMARITAN HOSP, DEPT MED, DIV MOLEC RHEUMATOL, BALTIMORE, MD, 21239; BECTON DICKERSON RES CTR, MT VIEW, CA, 94039; CORNELL UNIV, DEPT CHEM, ITHACA, NY, 14853. MOLECULAR IMMUNOLOGY (1991) Vol. 28, No. 10, pp. 1149-1154. Pub. country: USA. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Three rat **monoclonal antibodies** specific for mouse IgE (C12B9, 23G3, and B1E3) were established by using **monoclonal** anti-DNP mouse IgE (mIgE) as immunogen. These **antibodies**, as well as a fourth, R1E4, were characterized. It was found that one **antibody** (C12B9) recognizes an allotypic determinant (Igh-7a) found on the C-epsilon chain of mIgE. **Antibody** cross-blocking studies and epitope mapping studies using recombinant mIgE indicated that 3 **antibodies** (C12B9, R1E4 and 23G3) were directed against the C-epsilon-3 domain while one (B1E3) was directed against the C-epsilon-4 domain. A highly specific sandwich RIA for mIgE was developed using these **antibodies**. Use of these **monoclonal** anti-mIgE

antibodies in conjunction with recombinant chimeric mIgE-human **IgG1** molecules, demonstrated that the C-epsilon-3 domain is important in the binding of mIgE to the murine B cell Fc-epsilon-RII as well as to the murine mast cell Fc-epsilon-RI. The presence of the C-epsilon-4 domain influenced the binding of the recombinant IgE to the Fc-epsilon-RII; in contrast to the C-epsilon-4 domain had no effect on binding to the Fc-epsilon-RI.

L12 ANSWER 28 OF 35 CAPLUS COPYRIGHT 2003 ACS
1991:581023 Document No. 115:181023 Induction of intracellular calcium mobilization and cytotoxicity by hybrid mouse **monoclonal antibodies**. Fc.gamma.RII regulation of Fc.gamma.RI-triggered functions or signaling?. Koolwijk, Pieter; Van de Winkel, Jan G. J.; Pfefferkorn, Lorraine C.; Jacobs, Cor W. M.; Otten, Isabelle; Spierenburg, Gerrit T.; Bast, Bert J. E. G. (Dep. Mol. Biol. Biotechnol., Univ. Utrecht, Utrecht, Neth.). Journal of Immunology, 147(2), 595-602 (English) 1991. CODEN: JOIMA3. ISSN: 0022-1767.

AB The interaction was studied of bispecific mouse mAb with human IgG Fc receptors, and their ability was assessed to activate the monocytic cell line U937. Binding of monomeric hybrid anti-HuIgA1/HRP (horseradish peroxidase) mAb to the high-affinity IgG receptor, Fc.gamma.RI, on U937 cells was only obsd. when mAb with one or more mIgG2a H chains (hybrid mIgG1-2a, mIgG2a-2b, and mIgG2a-2a) were used. These Fc.gamma.RI-bound hybrid mAb were capable of enhancing the internal free cytosolic Ca2+ concn. ([Ca2+]i) in U937 cells only when bound mIgG was cross-linked using F(ab')2 fragments of goat anti-mIg **antibody**. A similar increase in [Ca2+]i was obsd. when Fc.gamma.R-bound hybrid mIgG1-2a mAb were cross-linked using goat anti-mIgG1 **antibody**, showing that the hybrid mAb themselves mediate the induction of Ca2+ increase. Remarkably, anti-Fc.gamma.RII mAb IV.3 was able to inhibit the Ca2+ increase induced via mIgG2a-1 or mIgG1-2a hybrid mAb completely, despite the fact that no effect of IV.3 on binding of monomeric hybrid mIgG1-2a or mIgG2a-1 mAb to U937 was detd. The hybrid mAb also induced lysis of HuIgA1-coated E using U937 effector cells. This lysis was completely inhibited by preincubation of U937 cells with mIgG2a mAb TB-3, which blocks Fc.gamma.RI via its Fc-part (Kurlander phenomenon). In contrast, Fc.gamma.RII-blocking mAb IV.3 and CIKM5 caused a significant enhancement of the **antibody** -dependent cellular cytotoxicity (ADCC) activity mediated by hybrid mIgG1-2a and mIgG2a-2b mAb. This enhancement did not occur when the parental anti-HuIgA1/2a or the hybrid anti-HuIgA1/HRP/2a-2a mAb were evaluated for ADCC activity. These findings suggest that hybrid mAb not only can bind to Fc.gamma.RI, but can mediate functional activation of myeloid cells. Given the effect of mAb IV.3 on [Ca2+]i changes and ADCC triggered through **IgG1**-2a mAb, Fc.gamma.RII may have a role in the regulation of Fc.gamma.RI-triggered functions or signaling.

L12 ANSWER 29 OF 35 MEDLINE
91100752 Document Number: 91100752. PubMed ID: 1824774. Suppression by IL-2 of IgE production by B cells stimulated by IL-4. Miyajima H; Hirano T; Hirose S; Karasuyama H; Okumura K; Ovary Z. (Division of Pathobiology, Juntendo University, School of Medicine, Tokyo, Japan.) JOURNAL OF IMMUNOLOGY, (1991 Jan 15) 146 (2) 457-62. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB IgE production was obtained from B cells of BALB/c or nude mice when these cells were cultured with IL-4 plus LPS. IL-2 added to these cultures at the start (day 0), 1 or 2 days later completely suppressed the production of IgE. The production of **IgG1** was also inhibited, but only if IL-2 was added on day 1. The production of other isotypes (IgM, IgG2a, IgG2b) was only slightly decreased by addition of IL-2. No suppression of IgE or **IgG1** production was observed if **monoclonal** anti-IL-2 was added, whereas anti-IFN-gamma had no effect on the suppression of the production of these isotypes. The expression of **CD23** on the third day of culture on B cells stimulated with LPS

and IL-4 was markedly decreased when IL-2 was added to the cultures on day 0. Addition of **monoclonal** anti-IL-2 suppressed all effects produced by IL-2, whereas addition of anti-IFN-gamma had no effect. These results show that the suppression by IL-2, at least for the first signaling processes, are different from the suppression produced by IFN-gamma.

L12 ANSWER 30 OF 35 MEDLINE
92035709 Document Number: 92035709. PubMed ID: 1834378. Cell-bound IgE and increased expression of Fc epsilon-receptors on dendritic cells in cutaneous infiltrates of mycosis fungoides. Preesman A H; Van de Winkel J G; Magnusson C G; Toonstra J; van der Putte S C; van Vloten W A. (Department of Dermatology, University Hospital Utrecht, The Netherlands.) CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1991 Nov) 86 (2) 246-51. Journal code: 0057202. ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Skin biopsies of 31 non-atopic patients, 20 with mycosis fungoides, six with psoriasis and five with contact dermatitis, and of five non-atopic healthy controls were compared for the presence of cell-bound IgE and vacant IgE binding sites. IgE+ cells were demonstrated in the cutaneous infiltrate of nine (45%) patients with mycosis fungoides, two (33%) with psoriasis and one (20%) with contact dermatitis. Following pre-incubation of skin sections with IgE myeloma protein to saturate vacant IgE-binding sites, 14 out of 16 patients (88%) with stage I mycosis fungoides, five (83%) patients with psoriasis and one (20%) with contact dermatitis showed an increase in the number of IgE+ cells. While cell-bound IgE was positively related to serum IgE levels the expression of IgE-binding sites was not. All IgE+ cells were HLA-DR+ dendritic cells identified as either macrophages (CD68+, CD14+) or Langerhans cells (CD1+). Skin biopsies of non-atopic healthy controls or clinically uninvolved skin in mycosis fungoides had neither any IgE+ cells nor any vacant binding sites. Inhibition studies with **IgG1**, IgG4 and IgE myeloma proteins as well as with several enzymatic fragments of IgE demonstrated that IgE interacted with Fc epsilon-receptors through isotype-specific structures on the Fc epsilon-fragment. Four anti-**CD23 monoclonal antibodies**, however, were unable to stain vacant Fc epsilon-receptors nor could they block IgE-binding. We hypothesize that locally-secreted lymphokines, like IL-4 or interferon-gamma, induce Fc epsilon-receptors on dendritic cells in the cutaneous infiltrate and that these receptors become occupied in parallel with elevated serum IgE levels.

L12 ANSWER 31 OF 35 MEDLINE
91006273 Document Number: 91006273. PubMed ID: 2145164. Induction of B cell activities by interleukin 4 is inhibited by a receptor-specific **monoclonal antibody** in vitro. Maliszewski C R; Sato T A; Vanden Bos T; Beckmann M P; Grabstein K H. (Department of Immunology, Immunex Corporation, Seattle, WA 98101.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1990 Aug) 20 (8) 1735-40. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB The effects of interleukin (IL) 4 on B cell growth and differentiation are mediated through binding of IL 4 to a specific cell surface receptor. The murine T cell IL 4 receptor (IL 4R) has recently been cloned and **monoclonal antibodies** (mAb) which bind specifically to the IL 4R have been developed. The ability of two of these anti-IL 4R mAb (M1 and M2') to inhibit IL 4-induced B cell functions in vitro was examined. The M1 mAb inhibited the ability of IL 4 to induce B cell proliferation in a dose-related fashion. The inhibition was specific for proliferation induced by IL 4 in that the **antibody** did not affect induction of proliferation by IL 1. Similarly, M1 inhibited IL 4-dependent B cell differentiation as measured by induction of **IgG1** and IgE secretion, decreased IgG1 secretion, increased Ia expression, and increased Fc epsilon R (**CD23**) expression. In

contrast, the anti-IL 4R-specific mAb M2 had no effect upon any of these activities. The ability of M1 but not M2 to inhibit IL 4-induced B cell growth and differentiation correlated with the inhibition of binding of radiolabeled IL 4 by M1. These reagents should be valuable tools with which to analyze the involvement of IL 4 in immune responses.

L12 ANSWER 32 OF 35 MEDLINE

90278143 Document Number: 90278143. PubMed ID: 2191049. Fc receptors of human Langerhans cells. Schmitt D A; Bieber T; Cazenave J P; Hanau D. (Laboratoire d'Histocompatibilite, Centre Regional de Transfusion Sanguine, Strasbourg, France.) JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1990 Jun) 94 (6 Suppl) 15S-21S. Ref: 36. Journal code: 0426720. ISSN: 0022-202X. Pub. country: United States. Language: English.

AB Receptors for the Fc fragment of immunoglobulins (Fc R) exhibit specificities for a wide variety of immunoglobulin classes and subclasses. In humans, at least three distinct classes of receptors for the Fc fragments of IgG (Fc gamma RI, II, III) and two classes of receptors for the Fc fragments of IgE (Fc epsilon RI, II) have been characterized. These classes were largely defined on the basis of their affinities for different immunoglobulin subclasses and their reactivities with **monoclonal** anti-receptor **antibodies**. Among these FcR, in healthy individuals, epidermal Langerhans cells (LC) express only the Fc gamma RII/CDw32. This FcR--a member of the immunoglobulin superfamily--is only present on about 50% of freshly isolated CD1a positive cells, as determined by rosette assays. It has a Mr of 40 kDa, is trypsin resistant, binds polymeric human IgG and murine **IgG1**-coated erythrocytes, and reacts with anti-CDw32 **monoclonal antibodies** (MoAb). LC internalize Fc gamma RII by receptor-mediated endocytosis. After 48 h of culture, human LC loose their Fc gamma RII, as revealed by flow cytometry. While the function(s) of the Fc gamma RII on human LC remain(s) unknown, this receptor may be primarily involved, like the Fc gamma RII present on mouse macrophages, in the clearance of extra-cellular immune complexes. In patients with atopic dermatitis having an elevated IgE serum level, beside an increased expression of the Fc gamma RII by LC located on lesional skin, IgE-bearing epidermal and dermal LC are present, again essentially on lesional skin. Double immunolabeling on cryosections reveals that on lesional skin only about 50% of the epidermal CD1a positive cells bear IgE. This capacity of LC to bind IgE molecules appears to be due to the presence of a specific Fc epsilon R. While the class of this Fc epsilon R still remains unclear, it appears to have some particularities: i) an associated expression with the CD1a antigen, ii) an affinity for IgG, and iii) a trypsin resistance. In vitro, human recombinant interleukin (IL)-4 and/or interferon (IFN)-gamma are able to induce the synthesis and expression of Fc epsilon RII/**CD23** on a percentage of normal human epidermal LC. This Fc epsilon RII seems to be functional since it binds IgE molecules, this binding being prevented by preincubation with anti-**CD23** MoAb. (ABSTRACT TRUNCATED AT 400 WORDS)

L12 ANSWER 33 OF 35 MEDLINE

90017517 Document Number: 90017517. PubMed ID: 2529541. Low-affinity IgE receptor (**CD23**) function on mouse B cells: role in IgE-dependent antigen focusing. Kehry M R; Yamashita L C. (Department of Immunology, DNAX Research Institute of Molecular and Cellular Biology, Inc., Palo Alto, CA 94304-1104.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1989 Oct) 86 (19) 7556-60. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB B-cell surface immunoglobulin very efficiently focuses specific protein antigens for presentation to T cells. We have demonstrated a similar role in antigen focusing for the low-affinity Fc epsilon receptor Fc epsilon RII on mouse B lymphocytes. B cells treated with an IgE **monoclonal antibody** to 2,4,6-trinitrophenyl TNP IgE-B cells were 100-fold more effective than were untreated B cells in

presenting low concentrations of TNP-antigen to T cells. Blocking the binding of IgE to Fc epsilon RII on IgE-B cells with a **monoclonal antibody** to Fc epsilon RII completely eliminated this increased effectiveness. Preformed complexes of IgE anti-TNP and TNP-antigen were more effectively presented (approximately 100-fold) than TNP-antigen in the presence of nonspecific IgE. In contrast, complexes of **IgG1** anti-TNP and TNP-antigen, capable of binding to Fc gamma receptors on B cells, were presented less effectively than TNP-antigen in the presence of nonspecific **IgG1**. Antigens focused by means of Fc epsilon RII or by means of B-cell surface immunoglobulin receptors were presented at comparably low concentrations. For several reasons, Fc epsilon RII on B lymphocytes seems to be particularly effective in efficiently focusing IgE-antigen complexes.

L12 ANSWER 34 OF 35 MEDLINE

89249392 Document Number: 89249392. PubMed ID: 2524281. Human peripheral blood T helper cell-induced B cell activation results in B cell surface expression of the **CD23** (BLAST-2) antigen. Crow M K; Kushner B; Jover J A; Friedman S M; Mechanic S E; Stohl W. (Department of Medicine, Hospital for Special Surgery, New York, New York.) CELLULAR IMMUNOLOGY, (1989 Jun) 121 (1) 99-112. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

AB We have developed an in vitro system to assess the early stages of B cell activation induced by peripheral blood T helper cells. Peripheral blood mononuclear cells are cultured for 16 hr with anti-CD3 **monoclonal antibody** (mAb), T lymphocytes are then removed by sheep red blood cell rosette depletion, and expression of the B cell surface activation antigen **CD23** (BLAST-2) is assessed by indirect immunofluorescence. Anti-CD3 mAb, but not a control anti-CD5 mAb, stimulates the expression of **CD23** on 20-50% of peripheral blood B cells cultured with autologous T cells. T cell subset depletion studies show that the CD4+ T cell subset is responsible for anti-CD3-mediated induction of **CD23** on autologous B cells. Anti-CD3-induced, T helper cell-dependent **CD23** expression is not MHC-restricted, as allogeneic combinations of T and non-T cells, cultured in the presence of anti-CD3 **antibody**, also result in the expression of B cell **CD23**. Individuals whose monocyte Fc receptors bind murine **IgG1** mAb poorly fail to trigger T cell proliferation in response to murine **IgG1** anti-CD3 mAb and also fail to express B cell **CD23** following culture of PBMC with **IgG1** anti-CD3 mAb, while the usual expression of **CD23** is seen after culture with IgG2a anti-CD3 mAb. The mechanism of anti-CD3-induced B cell activation was addressed in experiments using a two-chamber culture system. While little IL-4 activity was detected in anti-CD3-stimulated culture supernatants, optimal induction of **CD23** was observed when T and B cells were cultured together in a single chamber. This suggests that under physiologic conditions, in which quantities of lymphokine may be limiting, close physical contact between the anti-CD3-activated Th cell and B cell may be required for **CD23** expression. The anti-CD3-induced BLAST-2 assay will facilitate the analysis of Th cell-mediated B cell activation in any individual and should permit us to separately evaluate the roles of Th cells and B cells in the impaired immunoregulation characteristic of autoimmune disorders.

L12 ANSWER 35 OF 35 MEDLINE

89053481 Document Number: 89053481. PubMed ID: 2973449. Immunoglobulin E and immunoglobulin G subclass distribution in vivo and relationship to in vitro generation of interferon-gamma and neopterin in patients with severe atopic dermatitis. Reinhold U; Paweles G; Wehrmann W; Herold M; Wernet P; Kreysel H W. Immunology Laboratory, Medizinische Klinik, Tubingen, FRG. INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY, (1988) 87 (2) 120-6. Journal code: 9404561. ISSN: 0020-5915. Pub. country: Switzerland. Language: English.

AB In vitro interferon-gamma (IFN gamma) and neopterin generation by peripheral blood mononuclear cells (PBMC) from 15 patients with severe atopic dermatitis (AD) and 10 healthy controls was investigated. A significant proportion of patients had an impaired capacity to secrete IFN gamma after phytohemagglutinin (PHA) stimulation in vitro and therefore IFN gamma production was significantly lower compared to controls. Neopterin generation in vitro did not differ significantly from that of controls and no correlation between in vitro IFN gamma and neopterin production could be observed in either group. Analysis of serum IgG subclass distribution showed that patients with AD had increased IgG4 serum concentrations while **IgG1**, IgG2 and IgG3 levels did not differ significantly from those of controls. Surface marker analysis revealed increased numbers of **CD23**+ lymphocytes in patients with AD which was positively correlated with the serum IgG4 and IgE concentration. Furthermore, a significant correlation was found between IFN gamma generation in vitro and IgE and IgG4 concentration in vivo in AD. The data suggest that a possible dysregulation of IFN gamma, interleukin-4 or other lymphokine interleukin-4 or other lymphokine production may be related to increased IgE and IgG4 production and seems to be an important factor in the pathogenesis of AD.

=> d his

(FILE 'HOME' ENTERED AT 12:35:02 ON 06 JAN 2003)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 12:35:17 ON 06 JAN 2003

```
L1      2383121 S ANTIBODY
L2         3262 S L1 AND CD23
L3            0 S L2 AND HUMAN IGG1 CONSTANT
L4          182 S L2 AND IGG1
L5           76 S L4 AND HUMAN
L6            0 S L5 AND INHIBIT IGE
L7           67 DUP REMOVE L4 (115 DUPLICATES REMOVED)
L8            7 S L4 AND CHIMERIC
L9            3 DUP REMOVE L8 (4 DUPLICATES REMOVED)
L10          35 S L7 AND MONOCLONAL
L11           1 S L10 AND HUMANIZED
L12          35 DUP REMOVE L10 (0 DUPLICATES REMOVED)

=> s l2 and constant region
L13          13 L2 AND CONSTANT REGION

=> s l13 and IgG1
L14           1 L13 AND IGG1

=> d l14 cbib abs

L14 ANSWER 1 OF 1 SCISEARCH COPYRIGHT 2003 ISI (R)
96:695011 The Genuine Article (R) Number: VG477. AUTOANTIBODY-MEDIATED
     CAPTURE AND PRESENTATION OF AUTOANTIGEN TO T-CELLS VIA THE FC-EPSILON
     RECEPTOR BY A RECOMBINANT HUMAN AUTOANTIBODY FAB CONVERTED TO IGE. GUO J;
     QUARATINO S; JAUME J C; COSTANTE G; LONDEI M; MCLACHLAN S M; RAPOPORT B
     (Reprint). VET ADM MED CTR, THYROID MOL BIOL UNIT 111T, 4150 CLEMENT ST,
     SAN FRANCISCO, CA, 94121 (Reprint); VET ADM MED CTR, THYROID MOL BIOL UNIT
     111T, SAN FRANCISCO, CA, 94121; UNIV CALIF SAN FRANCISCO, SAN FRANCISCO,
     CA, 94121; MATHILDA & TERENCE KENNEDY INST RHEUMATOL, SUNLEY DIV, LONDON
     W6 8LW, ENGLAND. JOURNAL OF IMMUNOLOGICAL METHODS 29 SEP 1996 Vol. 195,
     No. 1-2, pp. 91-98. ISSN: 0022-1759. Pub. country: USA; ENGLAND. Language:
     ENGLISH.
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB      Fc epsilon receptor **CD23** -mediated capture of IgE-antigen
```

complexes by B cells provides a powerful antigen presenting system. Our goal was to develop a system using high affinity, human, organ-specific monoclonal autoantibodies for antigen capture by B cells, For this purpose, we converted a recombinant human autoantibody to TPO from a Fab (SP1.4) to an IgE molecule. Sera from all patients with autoimmune thyroid disease contain autoantibodies with the same epitope as SP1.4. The SP1.4 H and L chain V region genes were spliced by overlap PCR to a mammalian, non-immunoglobulin signal peptide and transferred to expression vectors for human **IgG1** and kappa, respectively. After inserting the IgE **constant region** genes into the H chain vector, the kappa and IgE H chain vectors were expressed in SP2/0 cells. SP1.4-IgE retains its high affinity (K-d) for TPO (similar to 2 x 10(-10) M), recognizes the same epitope as Fab SP1.4 and, importantly, binds to a different epitope than does Fab TR1.9. Binding of preformed complexes of SP1.4-IgE and biotinylated TPO to EB virus transformed B cells (EBVL) was weakly detectable by flow cytometry and was displaced by unlabeled TPO. SP1.4-IgE/I-125-TPO complex binding to EBVL was much more clearly evident, was also inhibited by the addition of unlabeled TPO, and was greatly reduced by preincubation of the EBVL with anti-**CD23**. Further, autologous EBVL preincubated with SP1.4-IgE/TPO complexes stimulated proliferation of TPO-specific T cells. IgE autoantibody-mediated antigen focusing to B cells is unlikely to operate in vivo but is, instead, a powerful investigative tool.

In conclusion, SP1.4-IgE is the first monoclonal human autoantibody to be developed for IgE-mediated antigen presentation to T cells by EBVL. Recombinant human autoantibodies converted to IgE, possibly in combinations if their epitopes permit simultaneous binding to the same molecule, provide a unique system to generate human T cell lines and clones specific for peptides naturally processed from internalized high affinity autoantibody/autoantigen complexes.

```
=> dup remove l13
PROCESSING COMPLETED FOR L13
L15             7 DUP REMOVE L13 (6 DUPLICATES REMOVED)

=> d l15 1-7 cbib abs

L15  ANSWER 1 OF 7      MEDLINE
2002224456  Document Number: 21957817.     PubMed ID: 11962725.    Anti-
     CD23 monoclonal antibody inhibits germline Cepsilon
     transcription in B cells. Yabuuchi Shingo; Nakamura Takehiko; Kloetzer
     William S; Reff Mitchell E. (Seikagaku Corporation, Central Research
     Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp) .
     Int Immunopharmacol, (2002 Mar) 2 (4) 453-61.  Journal code: 100965259.
     ISSN: 1567-5769. Pub. country: Netherlands. Language: English.
AB   A chimeric macaque/human (PRIMATIZED) anti-CD23 antibody
     , p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40
     antibody-stimulated IgE production by human peripheral blood
     mononuclear cells (PBMCs). RNA analysis by both reverse
     transcription-polymerase chain reaction (RT-PCR) and Northern blot showed
     that p6G5G1 inhibited germline Cepsilon RNA synthesis, but had no effect
     on CD23 mRNA levels. These data suggest that p6G5G1 may inhibit
     immunoglobulin class switching to IgE through the inhibition of germline
     Cepsilon RNA synthesis. Early addition of p6G5G1 after stimulation by IL-4
     and anti-CD40 was critical for IgE inhibition. In contrast, later addition
     of p6G5G1 still showed inhibition of increased levels of surface
     CD23, which is normally upregulated by stimulation with IL-4 and
     anti-CD40.

L15  ANSWER 2 OF 7      MEDLINE                                  DUPLICATE 1
2001150173  Document Number: 21150173.     PubMed ID: 11694997.    In vitro IgE
     inhibition in B cells by anti-CD23 monoclonal antibodies
```

is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB **CD23**, the low affinity receptor for IgE (FcvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal **antibodies** to human **CD23** were generated from cynomolgus macaques immunized with purified soluble **CD23** (sCD23). Four of the five primate **antibodies** blocked the binding of IgE complexes to **CD23** positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate **antibodies** were utilized to construct chimeric macaque/human (PRIMATIZED((R))) monoclonal **antibodies**. PRIMATIZED((R)) p5E8G1, containing human gamma 1 **constant region**, inhibited IgE production in vitro as efficiently as the parent primate **antibody**, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-**CD23** **antibody** in a dose dependent fashion. The murine monoclonal **antibody** MHM6 recognizes human **CD23** at a different epitope than primate **antibody** 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-**CD23** **antibodies** inhibit IgE production requires cross-linking of **CD23** to an IgG receptor. These data also imply that neither bivalent cross-linking of **CD23** alone or inhibition of **CD23** binding to its natural ligands is sufficient to inhibit IgE production.

L15 ANSWER 3 OF 7 MEDLINE

1998405747 Document Number: 98405747. PubMed ID: 9736340.

Interferon-gamma-induced factor binding to the interleukin-4-responsive element of CD23b promoter in human tonsillar mononuclear cells: role in transient up-regulation of the interleukin-4-induced CD23b mRNA. Park H J; So E Y; Lee C E. (Department of Biology and Institute of Basic Science, College of Natural Science, Sung Kyun Kwan Univ. Suwon, Korea.) MOLECULAR IMMUNOLOGY, (1998 Mar) 35 (4) 239-47. Journal code: 7905289. ISSN: 0161-5890. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Stimulation of human tonsillar mononuclear cells with interleukin-4 (IL-4) and interferon-gamma (IFN-gamma) rapidly induced the activation of distinct nuclear factors with different mobilities, both of which bind the IL-4 response element (IL-4RE) of CD23b promoter as examined by electrophoretic mobility shift assays (EMSA). Co-treatment of IL-4 and IFN-gamma induced, in addition to the two distinct complexes, a new complex with an intermediate mobility. The IL-4-induced complex reacted with anti-STAT (signal transducers and activators of transcription) 6, resulting in a supershift whereas the formation of the IFN-gamma-induced complex was inhibited by anti-STAT 1. The intermediate complex appeared to react with both anti-STAT 6 and anti-STAT 1. Although IFN-gamma alone did not induce **CD23** mRNA transcription, Northern blot analysis revealed a transient up-regulation of the IL-4-induced **CD23** mRNA by IFN-gamma within 2 h of IFN-gamma treatment in these tonsillar cells. The results suggest that the IL-4RE of the IL-4-inducible gene can accommodate both IL-4- and IFN-gamma-activated factors, such as STAT 6 and STAT 1, either in homodimeric or heterodimeric forms and the binding of these different proteins to the respective promoter may play a potential regulatory role in the IL-4-inducible gene expression.

L15 ANSWER 4 OF 7 MEDLINE

97131697 Document Number: 97131697. PubMed ID: 8977198. Analysis of the promoter elements necessary for IL-4 and anti-CD40 **antibody** induction of murine Fc epsilon RII (**CD23**): comparison with the germline epsilon promoter. Richards M L; Katz D H. (Division of Immunology, Medical Biology Institute, La Jolla, CA 92037, USA.) JOURNAL OF IMMUNOLOGY, (1997 Jan 1) 158 (1) 263-72. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB IL-4 and CD40 ligand stimulate transcription of **CD23** (Fc epsilonRII) in B cells and are necessary for the expression of germline epsilon mRNA and production of IgE. Because in vivo studies have shown that the Fc epsilonRII is involved in the regulation of IgE, a study was initiated to compare how IL-4 and engagement of CD40 up-regulate the Fc epsilonRII and epsilon genes. Herein, we describe the preparation of a series of linker-scanning mutants that cover the IL-4 response region in the murine Fc epsilonRII promoter, and their function when transfected into M12.4.5 and M12.4.1 B lymphoma cell lines. Several discrete elements were found to be necessary for IL-4 induction of the Fc epsilonRII gene, some of which have homology with the binding sites of known transcription factors, including NF-IL-4 and NF-kappaB. In contrast, the response element for anti-CD40 (plus IL-4) mapped to a single discrete sequence, a NF-kappaB-like site. Aligning the Fc epsilonRII and germline epsilon promoters in the region that is highly conserved between the human and mouse homologues of both genes reveals a high degree of identity, particularly within discrete clusters. Comparing the function of linker-scanning mutants of the Fc epsilonRII promoter with a similar report for germline epsilon shows that both genes require at least two homologous and similarly located DNA elements in their promoters for a full IL-4 induction. Moreover, the similar response of Fc epsilonRII and epsilon promoter-driven chloramphenicol acetyl transferase plasmids to several cytokines and other agents suggests that the two proximal promoter regions are activated by a similar cassette of factors.

L15 ANSWER 5 OF 7 SCISEARCH COPYRIGHT 2003 ISI (R)

96:685011 The Genuine Article (R) Number: VG477. AUTOANTIBODY-MEDIATED CAPTURE AND PRESENTATION OF AUTOANTIGEN TO T-CELLS VIA THE FC-EPSILON RECEPTOR BY A RECOMBINANT HUMAN AUTOANTIBODY FAB CONVERTED TO IGE. GUO J; QUARATINO S; JAUME J C; COSTANTE G; LONDEI M; MCLACHLAN S M; RAPOPORT B (Reprint). VET ADM MED CTR, THYROID MOL BIOL UNIT 111T, 4150 CLEMENT ST, SAN FRANCISCO, CA, 94121 (Reprint); VET ADM MED CTR, THYROID MOL BIOL UNIT 111T, SAN FRANCISCO, CA, 94121; UNIV CALIF SAN FRANCISCO, SAN FRANCISCO, CA, 94121; MATHILDA & TERENCE KENNEDY INST RHEUMATOL, SUNLEY DIV, LONDON W6 8LW, ENGLAND. JOURNAL OF IMMUNOLOGICAL METHODS (09 SEP 1996) Vol. 195, No. 1-2, pp. 81-92. ISSN: 0022-1759. Pub. country: USA; ENGLAND. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Fc epsilon receptor (**CD23**)-mediated capture of IgE-antigen complexes by B cells provides a powerful antigen presenting system. Our goal was to develop a system using high affinity, human, organ-specific monoclonal autoantibodies for antigen capture by B cells, For this purpose, we converted a recombinant human autoantibody to TPO from a Fab (SP1.4) to an IgE molecule. Sera from all patients with autoimmune thyroid disease contain autoantibodies with the same epitope as SP1.4. The SP1.4 H and L chain V region genes were spliced by overlap PCR to a mammalian, non-immunoglobulin signal peptide and transferred to expression vectors for human IgG1 and kappa, respectively. After inserting the IgE **constant region** genes into the H chain vector, the kappa and IgE H chain vectors were expressed in SP2/0 cells. SP1.4-IgE retains its high affinity K-d for TPO similar to 2 x 10 -10 M , recognizes the same epitope as Fab SP1.4 and, importantly, binds to a different epitope than does Fab TR1.9. Binding of preformed complexes of SP1.4-IgE and biotinylated TPO to EB virus transformed B cells EBVL was weakly detectable by flow cytometry and was displaced by unlabeled TPO. SP1.4-IgE/I-125-TPO complex binding to EBVL was much more clearly evident,

was also inhibited by the addition of unlabeled TPO, and was greatly reduced by preincubation of the EBVL with anti-**CD23**. Further, autologous EBVL preincubated with SP1.4-IgE/TPO complexes stimulated proliferation of TPO-specific T cells. IgE autoantibody-mediated antigen focusing to B cells is unlikely to operate in vivo but is, instead, a powerful investigative tool.

In conclusion, SP1.4-IgE is the first monoclonal human autoantibody to be developed for IgE-mediated antigen presentation to T cells by EBVL. Recombinant human autoantibodies converted to IgE, possibly in combinations if their epitopes permit simultaneous binding to the same molecule, provide a unique system to generate human T cell lines and clones specific for peptides naturally processed from internalized high affinity autoantibody/autoantigen complexes.

L15 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS
1991:653735 Document No. 115:253735 Monoclonal **antibodies** defining epitopes on human IgE. Hook, William A.; Zinsser, Frank U.; Berenstein, Elsa H.; Siraganian, Reuben P. (Lab. Immunol., Natl. Inst. Dent. Res., Bethesda, MD, 20892, USA). Molecular Immunology, 28(6), 631-9 (English) 1991. CODEN: MOIMD5. ISSN: 0161-5890.

AB Twelve monoclonal **antibodies** (mAb) were isolated that bound to 6 clusters of epitopes on the **const. region** of the epsilon chain of human IgE. Four of the mAb bound to the C.epsilon.1 or early C.epsilon.2 regions; 3 of these bound to the IgE myeloma protein PS and to serum IgE but not to the IgE myeloma protein ND. These mAb probably recognize an allotypic marker. Another mAb reacted with heat-denatured, but not native IgE. Four of the mAb failed to release histamine; the epitopes recognized by these mAb are in the C.epsilon.1, C.epsilon.2 and C.epsilon.3-4 regions of IgE. Three of these non-histamine releasing mAb did not bind to IgE on the basophil surface. These mAb recognize epitopes in C.epsilon.2 and C.epsilon.3-4 that are not accessible when IgE is bound to its receptor. Four mAb inhibited IgE binding to basophils; 2 of these did not release histamine, and 2 others that bind to epitopes in the C.epsilon.2-4 domain, released histamine and therefore blocked IgE binding by steric hindrance. Inhibition of IgE binding by different mAb suggest that the Fc.epsilon.RI and Fc.epsilon.RII bind to partly overlapping regions of the IgE mol. although the sites do not appear to be identical. A no. of sites of C.epsilon.1 and C.epsilon.3-4 were accessible when IgE is bound to its basophil receptor. The data support the concept that only part of the Fc portion of IgE is hidden in the receptor and that portions of C.epsilon.1-4 are accessible on the cell surface. These mAb should be useful in detg. the domains of IgE that are crit. for its biol. activity.

L15 ANSWER 7 OF 7 MEDLINE DUPLICATE 2
88270763 Document Number: 88270763. PubMed ID: 2968873. Expression of Fc epsilon receptors and surface and cytoplasmic IgE on human fetal and adult lymphopoietic tissue. Kanowith-Klein S; Hofman F; Saxon A. (Department of Medicine, UCLA, Los Angeles, California 90024.) CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, (1988 Aug) 48 (2) 214-24. Journal code: 0356637. ISSN: 0090-1229. Pub. country: United States. Language: English.

AB The appearance during ontogeny of IgE-positive and Fc epsilon receptor (FcER)-bearing cells was studied. Monoclonal **antibody** to the **constant region** (Fc) of IgE (CIA-E-7.12) was used to detect cytoplasmic and surface IgE. A monoclonal **antibody** to the low-affinity Fc epsilon receptor (FcER-II = **CD23**) and immune complexes composed of human IgE and mouse monoclonal anti-human IgE Fc were used to detect FcER. Cryostat sections of human fetal tissues (liver, lung, spleen, and thymus) from 11 to 22 weeks gestation as well as adult tonsil tissues were examined for IgE, FcER, and other lymphoid markers by immunoperoxidase staining. Although both IgE- and FcER-positive cells were present in adult tissues, we found that, in contrast to an earlier report, such cells were not present in the fetal tissues examined. The in situ

location of FcER on cells in human lymphoid tissues revealed that the FcER-bearing cells were localized predominantly in the germinal centers (mature B cell and macrophage areas) of the tonsil follicles with some staining in the mantle (resting and less mature B cell areas).

=> s inhibit IgE
L16 998 INHIBIT IGE

=> s l16 and antibod?
L17 466 L16 AND ANTIBOD?

=> s l17 and human CD23
3 FILES SEARCHED...
L18 11 L17 AND HUMAN CD23

=> dup remove l18
PROCESSING COMPLETED FOR L18
L19 3 DUP REMOVE L18 (8 DUPLICATES REMOVED)

=> d l19 1-3 cbib abs

L19 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2002:370946 Document No.: PREV200200370946. **Antibodies** against the stalk region of huCD23 block binding of IgE and inhibit in vitro IgE synthesis. Caven, Timothy Hays (1); Ma, Check (1); Beavil, Rebecca; Beavil, Andrew; Ghirlando, Rodolpho; Gould, Hannah; Conrad, Daniel (1). (1) Virginia Commonwealth University, 1217 East Marshall Street, Richmond, VA, 23298 USA. FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1239. http://www.fasebj.org/. print. Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language: English.
AB The stalk region of **human CD23** comprising a.a. 48-153 was expressed in E. coli and purified. In addition a chimeric **human CD23** was prepared consisting of the extracellular region of CD23 linked to a modified leucine zipper (LZ-CD23). Polyclonal antisera were produced in rabbits and shown to block binding of IgE to CD23 both on cell surfaces as well as the interaction of LZ-CD23 with IgE in an ELISA based assay. The antisera was also shown to **inhibit IgE** synthesis in an anti-CD40/IL-4 stimulated human PBL model. The inhibition was dose dependent and essentially complete blockage of IgE production was seen at a relatively low dose of anti-stalk. FACS analysis using CD23+B lymphoblastoid cells indicated little if any endocytosis and/or protection from cleavage induced by the anti-stalk. Monoclonal **antibodies** against the human stalk have also been prepared and these are being analyzed for the capacity to **inhibit IgE** binding and IgE synthesis, as well as compare their efficacy to the anti-lectin mabs. The results indicate that targeting the stalk region is efficacious with respect to blocking IgE production.

L19 ANSWER 2 OF 3 MEDLINE DUPLICATE 1
2001209686 Document Number: 21195373. PubMed ID: 11298826.
Metalloprotease inhibitor-mediated inhibition of mouse immunoglobulin production. Kilmon M A; Mayer R J; Marshall L A; Conrad D H. (Virginia Commonwealth University, Department of Microbiology and Immunology, Richmond, VA 23298, USA.. mkilmon@hsc.vcu.edu . IMMUNOLOGY, 2001 Mar 102 (3) 281-9. Journal code: 0374672. ISSN: 0019-2805. Pub. country: England: United Kingdom. Language: English.
AB High levels of membrane CD23 have been shown to decrease immunoglobulin E IgE . CD23 is a very labile molecule and is cleaved from the cell surface by an unknown metalloprotease. Two metalloprotease inhibitors, compound A N-[4-hydoxyamino-2- R -isobutyl-3- S propargylthiomethylsuccinyl]- S - phenylalnine-N'-methyl-amide and compound B N-[3- S -hydroxy-4-

hydroxyamino-2-(R)-(2-naphthylmethyl) succinyl]-(S)-tert-leucinamide), were chosen for their ability to inhibit **human CD23** cleavage and selectively **inhibit IgE** production. The ability of these inhibitors to block cleavage of murine CD23 and immunoglobulin production in an in vitro system was examined. The inhibitors blocked sCD23 release from B cells. The inhibitors also decreased IgE production by B cells; however, 20-30 times more inhibitor was needed to give a similar amount of inhibition as compared with sCD23 release. The effects on immunoglobulin production did not require the presence of CD23 in that these inhibitors also blocked in vitro immunoglobulin production when B cells from CD23-/- mice were used. The inhibitors decreased production of all other immunoglobulin isotypes examined and reduced the number of IgE **antibody**-forming cells (AFC) while having no effect on cell proliferation or viability. The level of Iepsilon transcripts in cells treated with compounds A and B were not different as compared with control cells. These results suggest that while these inhibitors effectively **inhibit IgE** production in a CD23-specific manner in the human, these compounds, in the mouse, inhibit immunoglobulin production by an unknown mechanism that is unrelated to CD23.

L19 ANSWER 3 OF 3 MEDLINE DUPLICATE 2

2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-CD23 monoclonal **antibodies** is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for IgE (FcvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal **antibodies** to **human CD23** were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate **antibodies** blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate **antibodies** were utilized to construct chimeric macaque/human (PRIMATIZED((R))) monoclonal **antibodies**. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate **antibody**, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not **inhibit IgE** production but did interfere with IgE inhibition by the intact anti-CD23 **antibody** in a dose dependent fashion. The murine monoclonal **antibody** MHM6 recognizes **human CD23** at a different epitope than primate **antibody** 5E8, and **inhibits IgE** production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to **inhibit IgE** production. These data imply that the mechanism by which anti-CD23 **antibodies inhibit IgE** production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to **inhibit IgE** production.

=> s primate CD23
L20 1 PRIMATE CD23

=> d l20 cbib abs

L20 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
2002:594704 Document No. 137:153822 CD23 antagonistic antibodies for treatment of neoplastic disorders. Hariharan, Kandasamy; Hanna, Nabil; Braslawsky, Gary R.; Pathan, Nuzhat (Idec Pharmaceuticals Corporation, USA). PCT Int. Appl. WO 2002060484 A1 20020808, 88 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US2620 20020131. PRIORITY: US 2001-772938 20010131; US 2001-855717 20010516; US 2001-985646 20011105.

AB Methods and kits for the treatment of neoplastic disorders comprising the use of a CD23 antagonist are provided. These CD23 antagonists are monoclonal, polyclonal, chimeric, humanized or primatized antibodies, e.g. IDEC-152. The CD23 antagonist may be used alone or in combination with radiotherapeutic or chemotherapeutic agents. In particularly preferred embodiments the CD23 antagonists may be used to treat B cell chronic lymphocytic leukemia (B-CLL).

=> s (reff M?/au or kloetzer w?/au or nakamura t?/au)
L21 44002 (REFF M?/AU OR KLOETZER W?/AU OR NAKAMURA T?/AU)

=> s l21 and CD23 antibody
L22 11 L21 AND CD23 ANTIBODY

=> dup remove l22
PROCESSING COMPLETED FOR L22
L23 3 DUP REMOVE L22 (8 DUPLICATES REMOVED)

=> d l23 1-3 cbib abs

L23 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
2002224456 Document Number: 21957817. PubMed ID: 11962725. Anti-CD23 monoclonal antibody inhibits germline Cepsilon transcription in B cells. Yabuuchi Shingo; **Nakamura Takehiko; Kloetzer William S ; Reff Mitchell E.** (Seikagaku Corporation, Central Research Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp) . Int Immunopharmacol, (2002 Mar) 2 (4) 453-61. Journal code: 100965259. ISSN: 1567-5769. Pub. country: Netherlands. Language: English.

AB A chimeric macaque/human (PRIMATIZED) anti-**CD23 antibody** , p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40 antibody-stimulated IgE production by human peripheral blood mononuclear cells (PBMCs). RNA analysis by both reverse transcription-polymerase chain reaction (RT-PCR) and Northern blot showed that p6G5G1 inhibited germline Cepsilon RNA synthesis, but had no effect on CD23 mRNA levels. These data suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE through the inhibition of germline Cepsilon RNA synthesis. Early addition of p6G5G1 after stimulation by IL-4 and anti-CD40 was critical for IgE inhibition. In contrast, later addition of p6G5G1 still showed inhibition of increased levels of surface CD23, which is normally upregulated by stimulation with IL-4 and anti-CD40.

L23 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
2000150073 Document Number: 20150073. PubMed ID: 10694997. In vitro IgE inhibition in B cells by anti-CD23 monoclonal antibodies is functionally dependent on the immunoglobulin Fc domain. **Nakamura T; Kloetzer W S**; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J;

Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; **Reff M E.**
(Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.)
INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41.
Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for IgE (FcvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED((R))) monoclonal antibodies. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-**CD23 antibody** in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-**CD23 antibodies** inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

L23 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS

1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. **Reff, Mitchell R.**; Barnett, Richard Spence; McLachlan, Karen Retta (Idec Pharmaceuticals Corporation, USA). U.S. US 5998144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSO cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors Molly and vector combinations for use in the subject cloning method are also provided. This Molly vector contains dihydrofolatereductase, N1+Neomycin phosphotransferase exon1, N2+Neomycin phosphotransferase exon 2, anti-CD23 light chain leader+variable, human kappa const., anti-CD23 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and polioma enhancer, mouse beta

globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and Anti-human **CD23** **antibody** and immunoadhesin in Desmond marked CHO cells was achieved.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	241.79	242.00

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-11.07	-11.07

STN INTERNATIONAL LOGOFF AT 12:43:33 ON 06 JAN 2003